DESIGN AND SYNTHESIS OF 1*H*-PYRAZOLO[3,4-*b*]PYRIDIN-3(2*H*)-ONES AND CORRESPONDING N-NUCLEOSIDES - NEW PURINE ISOSTERS AS POTENTIAL DRUG-LIKE SCAFFOLDS

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Linda Supe

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Abstract

The present work is devoted to study synthesis and modification of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones, which could result in appearance of a number of biological activities. 1*H*-Pyrazolo[3,4-*b*]pyridin-3(2*H*)-one derived moieties and their modifications were prepared using classical approaches involving [3+3] cyclocondensations of enamine containing heterocycles and bielectrophiles, inverse electron-demand Diels-Alder reactions, and palladium-catalyzed C-C coupling reactions. *N*-Nucleosides of purine analogues were synthesized using a modified silyl Hilbert-Jones method while acyclic nucleoside analogues were obtained using *N*-alkylation with alkyl bromides. Scope and limitations of the hydrogenation of the pyridine ring of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones were studied.

Kurzbeschreibung

Die vorliegende Arbeit untersucht Synthese und Modifikation von 1*H*-Pyrazolo[3,4-*b*]pyridin-3(2*H*)-onen, die potentielle biologische Aktivität zeigen können. 1*H*-Pyrazolo[3,4-*b*]pyridin-3(2*H*)-one und deren Derivate wurden durch [3+3] Zyklokondensation von Enamin-enthaltenden Heterozyklen und Bielektrophilen, durch Diels-Alder Reaktionen mit inversem Elektronenbedarf sowie durch Palladium katalysierte Kupplungsreaktionen synthetisiert. *N*-Glykolysierte Purine wurden nach einer modifizierten Silyl Hilbert-Jones Methode synthetisiert. Die entsprechenden azyklischen Derivate wurden durch *N*-Alkylierung mit Bromalkanen gewonnen. Anwendungsbreite und Grenzen der Hydrierung von 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-onen wurden untersucht.

Abbreviations

Ac	Acetyl
ADA	Adenosine deaminase
AIDS	Acquired immunodeficiency syndrome
BSA	N,O-bis(trimethylsilyl)acetamide
COSY	Correlation spectroscopy
DMF	N,N-dimethylformamide
DMSO	Dimethylsulphoxide
DNA	Desoxyribonucleic acid
EI	Electron ionization
ESI	Electron spray ionization
Et	Ethyl
EtOH	Ethanol
GC	Gas chromatography
h	Hours
HIV	Human immunodefficiency virus
HRMS	High resolution mass spectroscopy
HMBC	Heteronuclear Multiple Bond Correlation
HSQC	Heteronuclear Single Quantum Correlation
Hz	Hertz HRMS
IMPDH	Inosine monophosphate dehydrogenase
i-Pr	Isopropyl
IR	Infrared
m	meta
Me	Methyl
MeOH	Methanol
mp	Melting point
MS	Mass spectroscopy
NADH	Nicotinamide adenine dinucleotide
NBS	N-Bromosuccinimide
NMR	Nuclear magnetic resonance
NOESY	Nuclear Overhauser effect spectroscopy
o	ortho
p	para

Ph	Phenyl
PTSA	p-Toluenesulphonic acid
RNA	Ribonucleic acid
RT	Room temperature
SCID	Severe combined immunodeficiency
t-Bu	*tert*-Butyl
TEA	Triethylamine
Tf	Triflate
TMS	Trimethylsilyl
TMSOTf	Trimethylsilyl trifluromethanesulphonate
TLC	Thin layer chromatography
TPPTS	Sodium triphenylphosphine trisulfonate

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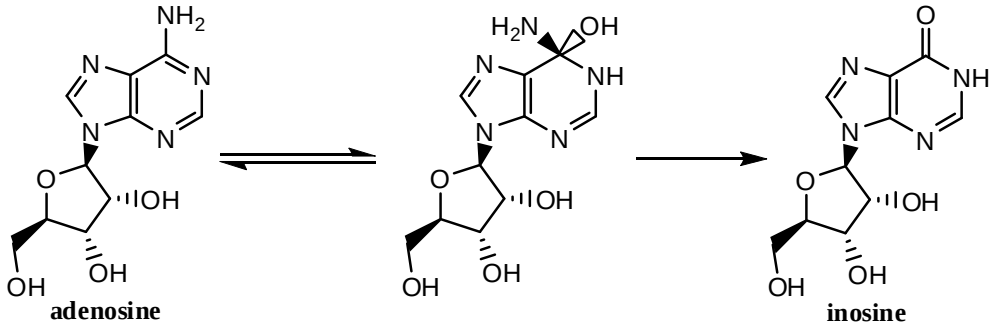
1. Background

Purines, pyrimidines and their nucleosides are building blocks of DNA and RNA and therefore possess a fundamental importance in all living systems.[1,2] They have been playing a major role in treating tumors and viruses, and act as selective inhibitors of certain obligatory enzymes for cancer or viral replication[3], or as nucleic acid chain terminators which interrupt the replication of cancer cells or a virus.[4] The emergence of acquired immunodeficiency syndrome (AIDS) stimulated extensive antiviral research in the past several decades. The study of anti-HIV chemotherapy has promoted a rapid progress of medicinal chemistry, molecular virology as well as an understanding of the mechanism of action of antiviral agents. Among the medicals currently approved for the treatment of AIDS, hepatitis B and C, and infections by herpes viruses, nucleoside analogs play a major role.

1.1. Some important members of the enzyme family

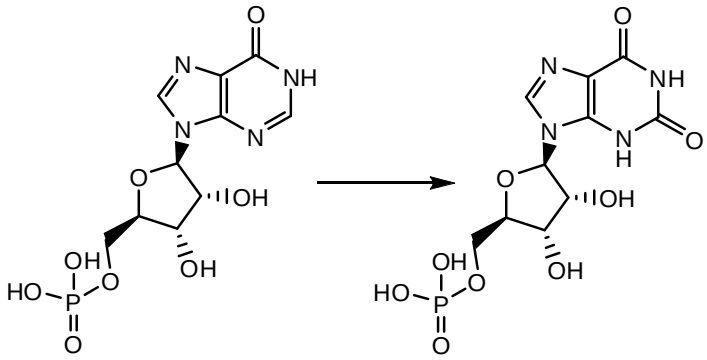
Adenosine deaminase (**ADA**) and **Inosine-5′-monophosphate dehydrogenase** (**IMPDH**) are considered one of the key enzymes of purine metabolism.[5] ADA catalyses deamination of adenosine to inosine via formation of covalent hydrate: [5b,c]



Scheme 1. Adenosine deamination catalyzed by ADA.

Present in virtually all mammalian cells, primary function of ADA is the development and maintenance of the immune system.[5c] ADA association has also been observed with epithelial cell differentiation, neurotransmission, and gestation maintenance.[6] It has also been proposed that ADA, in addition to adenosine breakdown, stimulates release of excitatory amino acids

and is necessary to the coupling of A1 adenosine receptors and heterotrimeric G proteins.[5b] Meanwhile, IMPDH has an essential role in providing precursors for DNA and RNA bioysynthesis.[6] IMPDH catalyzes oxidation of inosine monophosphate to xanthosine monophosphate:



Scheme 2. IMPDH catalyzed oxidation of inosine monophosphate.

IMPDH also plays a role in signal transduction pathways that mediate cell differentiation. As purine metabolism is largely conserved across all known organisms, so is the structure and function of IMPDH.[5d,7]

Both ADA and IMPDH enzymes recently became important targets for drug design,[8] since it was found that dysfunction of ADA and IMPDH is involving many diseases including AIDS,[9] severe combined immunodeficiency (SCID),[10] tuberculosis,[11] Parkinson's disease,[12] viral hepatitis,[13] autism,[14] bacterial meningitis [15] and several forms of cancer.[16]

Deficient levels of ADA have also been associated with pulmonary inflammation, thymic cell death, and defective T-cell receptor signaling.[17] Conversely, mutations causing this enzyme to be overexpressed are one cause of hemolytic anemia.[18]

IMPDH expression is found to be upregulated in tumor tissues and tumor cell lines.[19]

1.2. Antimetabolites

Design and synthesis of antimetabolites – substances bearing a close structural resemblance to those required for normal physiological functioning – is one of most popular strategies of drug development. Antimetabolite drugs were among the first effective chemotherapeutic agents discovered so far. Generally, antimetabolites are purine, pyrimidine or folic acid analogues; they induce cell death during the S phase of cell growth when incorporated into RNA and DNA or inhibit enzymes needed for nucleic acid production.[20]

Few examples of antimetabolites are outlined in **Figure 1**. **Cytarabine** is a chemotherapy agent used mainly in the treatment of cancers of white blood cells such as acute myeloid leukemia and non-Hodgkin lymphoma.[21] Cytarabine mimics **deoxycitidine**, a component of DNA, and is the first of a series of cancer drugs that altered the sugar component of nucleosides instead of base.[22] **Tenofovir** is a useful drug in HIV-1 treatment,[23] while **nelarabine** is a chemotherapy drug used in T-cell acute lymphoblastic leukemia. **Acyclovir** is one of the most commonly used antiviral drugs, primarily used for the treatment of herpes simplex virus infections.[24] **Mercaptopurine** is used to treat leukemia,[25] psoriatic arthritis,[26] and inflammatory bowel disease (such as Crohn's disease and ulcerative colitis).[27] It has demonstrated some *in vitro* effectiveness against *Mycobacterium paratuberculosis*.[28]

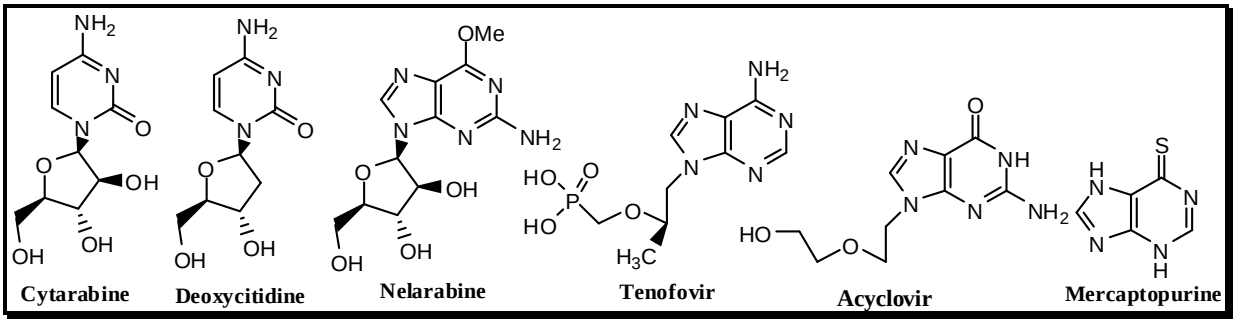


Figure 1. Antimetabolites used in pharmacy.

1.3. Design of purine isosteres

Bioisosteric replacements in organic molecules have been broadly studied to understand their affect on several parameters including size of the molecule, conformation, inductive and mesomeric effects, polarizability, H-bond formation capacity, pKa, solubility, hydrophobicity, reactivity, stability.[29] Bioisosterism represents one approach used for the rational modification of lead compounds in order to increase selectivity, stability, improve pharmacokinetics (solubility-hydrophobicity). Biosterically modified compounds often have decreased toxicity and less side effects when interacting with target enzyme compared to parent compounds.[30]

One of the most common and powerful isosteric replacements is substitution of hydrogen by fluorine. Selective introduction of fluorine into a bioactive substance as an isosteric replacement of hydrogen or as an isopolar mimic of hydroxyl group, frequently leads to a dramatic change in biological activities and becomes an important strategy in the design and

discovery of novel drug candidates. The impact rendered by fluorine on molecular properties has been well studied and described in the literature.[31-33]

The reason for the incorporation of one or more fluorine atoms into biologically active molecules is based on the following characteristics of fluorinated compounds: [1, 31-33]

1) fluorine is the second smallest atom and closely mimics hydrogen without much distortion of the geometry;

2) fluorine is the most electronegative element which can serve as an isopolar and isosteric mimic of a hydroxyl group since the C–F bond length (1.35 Å) is close to the C–O bond length (1.43 Å), as well as fluorine is a hydrogen-bond acceptor;

3) strength of the C–F bond exceeds that of the C–H bond which often results in increased biological and chemical stability of organofluorine compounds. Therefore fluorine can be placed on easily oxidized positions to increase stability during metabolic processes.

Instead of fluorine alone, the trifluoromethyl group CF_3 may be used as alternative electron-withdrawing group.[1, 29a] In fact, the trifluoromethyl group is considered as isosterically close to the amino group (NH_2),[31c,e] and many enzymes tolerate the exchange of an amino by a trifluoromethyl group. At the same time, the structural fragment CF_2 which is sterically similar to the CH_2 group, contrasting sharply with the latter in polarity and reactivity.[34] In particular, CF_2 is thought to be an isopolar and isosteric substitute for oxygen.[35]

The occurrence of a fluorine substituent in commercial pharmaceutical compounds continues to increase by 2% in 1970 to about 20-25% at present. The figures are higher (currently above 28%) in agrochemicals.[32a] To date there are known more than 200 pharmaceuticals with at least one fluorine substituent.[31b, 32b] This is a high number considering that fluoroorganic compounds are almost absent from nature. Countless yet still appearing reports and reviews [31-33] emphasize the significance and actuality of organofluorine chemistry.

Introduction of fluorine into an organic molecule can be performed by direct selective fluorination of target or by the building block method, when fluorinated intermediates are used in cyclisation reactions.[36-39] Some of the common fluorinating agents are shown in **Figure 2**:

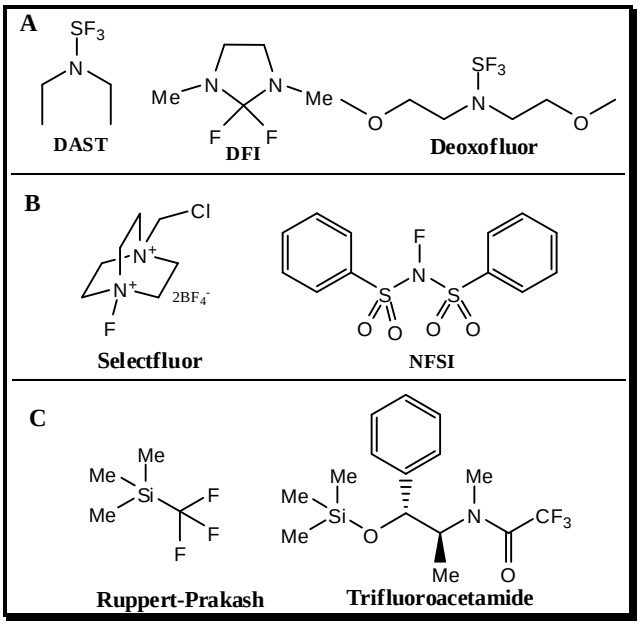


Figure 2. Examples of safe and selective fluorination agents. (**A**) Nucleophilic agents; (**B**) electrophilic agents, and (**C**) reagents to introduce CF_3 groups.

In nucleoside chemistry, **Selecfluor** is widely used to introduce a fluorine atom into heterocyclic bases via electrophilic substitution.[40,41] Selecfluor can also selectively fluorinate certain sugar moieties, which possess electron-rich double bonds via an electrophilic addition.[42,43] Meanwhile, **DAST** is the most versatile reagent for fluorination of sugar moiety – it provides a one-step exchange of a hydroxyl group by fluorine. It can replace primary, secondary, tertiary and allylic hydroxyl groups by fluorine in excellent yields. For most substrates, S_N2 displacement of hydroxyl by fluorine occurs with a complete inversion of configuration. DAST can also convert most aldehydes and ketones to the corresponding gem-difluorides.[33a, 44]

1.4. Fluorinated nucleosides

Fluoroorganic molecules are rare in nature, while naturally occurring fluorinated nucleosides are even more uncommon. **Nucleocidin** (**Figure 3**) is the first naturally occurring derivative of a fluoro sugar.[45, 46] It was first isolated as an anti-trypanosome antibiotic from the fermenatation broth of *Streptomices calvus*.[47,48]

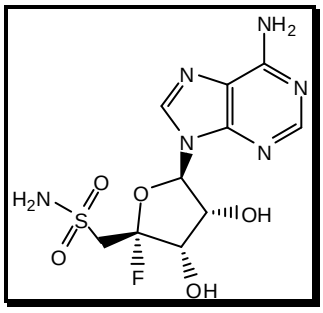


Figure 3. Nucleocidin - natural fluorinated nucleoside.

Introduction of at least one fluorine atom either into sugar or heterocyclic part usually leads to transformation of natural or less active synthetic nucleosides into fluoro derivatives bearing pharmacologically attractive properties.[49-53]

Fluorine is an obvious choice for incorporating into sugar-modified nucleoside analogues, since fluorine can be considered as reasonable mimic of either a hydrogen atom or a hydroxyl group. There has been a significant amount of research into fluorinated nucleoside analogues as potential treatments for cancer and viral infection.[54-63]

Currently several potent anti-viral and anti-cancer fluorinated nucleosides and their precursors are widely used. **Fludarabine** phosphate[31f, 64] is an excellent example of the influence of fluorine on molecule. Fludarabine is a fluorinated analog of a purine nucleoside antiviral agent **vidarabine**. The disadvantage of vidarabine is that it is prone to deamination by ADA. The metabolite hypoxantine still possesses antiviral activity, but is 10-fold less potent than vidarabine.[65] Unlike vidarabine, fludarabine is resistant to deamination by adenosine deaminase, thanks to stabilizing effect of fluorine. Fludarabine is successfully used for treatment of several types of leukemias and lympfomas.[66-69] **Figure 4** shows the variety of commercial fluorinated drugs.

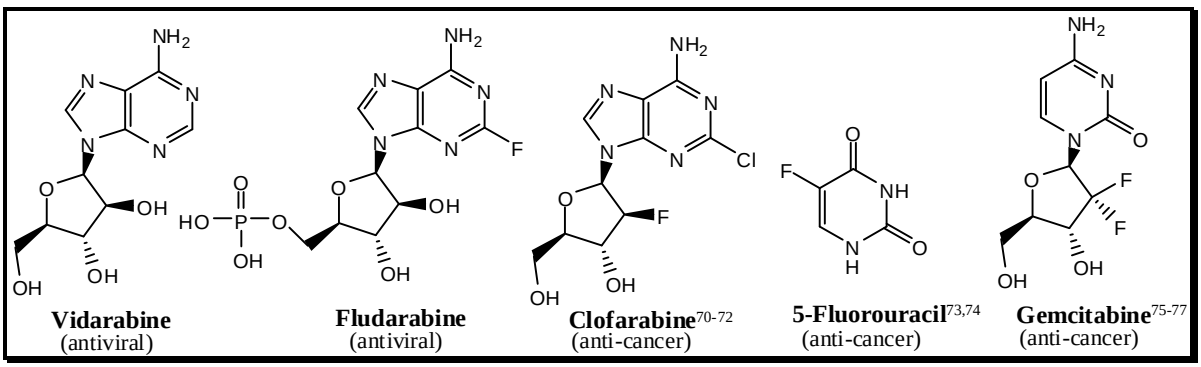


Figure 4. Popular fluorinated antiviral and anti-cancer drugs.

Many aspects of the chemistry of fluorinated nucleosides have been investigated in last decades focusing generally on the synthesis of fluorinated nucleosides that contain a fluorinated glykone moiety. Several excellent reviews have been published concentrated mainly on sugar-fluorinated nucleosides.[33a,49,78]

Nucleosides bearing a highly fluorinated moieties deserve a special attention. Nucleic acid-based fluorinated derivatives, e.g., nucleosides or oligonucleotides connected to highly fluorinated chains, have been investigated recently due to their high potential for biomedical applications. It has been reported that highly fluorinated derivatives possess unique properties, including chemical and biological inertness, strong hydro- and lipophobia.[79,80] Due to their unique properties, fluorocarbon chains represent a useful building block for the construction of supramolecular systems. Perfluoroalkyl chains have a larger cross section and are more rigid than their hydrogenated counterparts. They are considerably more hydrophobic and are lipophobic as well. As a result, when dispersed in water, fluorinated amphiphiles exhibit an enhanced capacity to self-assemble into highly stable and well-defined assemblies such as films, membranes, micelles, vesicles and other stable supramolecular systems.[81]

Highly fluorinated chains enhance stability, low permeability to both hydrophilic and lipophilic material and reduce interaction with biological media. These fluorinated amphiphiles possess a considerable potential for the delivery of materials such as drugs, prodrugs, markers, contrast agents and nucleic acids.[82] Recently, group of Barthélémy reported on the synthesis and biological properties of oligonucleotides bearing polyflouroalkyl-chain (**Figure 5**).[83] It was reported that conjugation of fluorocarbon chain to the oligonucleotide allows the delivery of highly polyanionic oligonucleotides into human cells, while incorporation of non-fluorinated analogues in cells was unsuccessful.

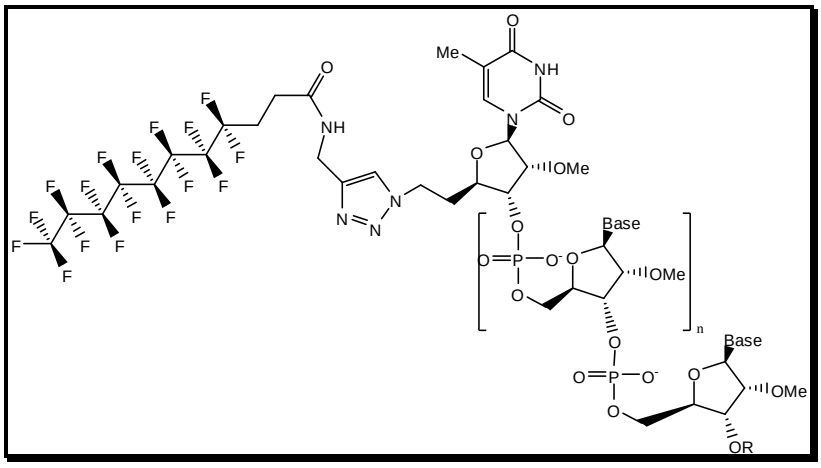


Figure 5. Polyfluorinated oligonucleotide.

1.5. Goals and tasks of current work

The amount of manuscripts and reviews still appearing on nucleoside and fluorine chemistry clearly indicates the actuality of the field. The group of Professor Langer has made a great contribution in progress of fluorine and nucleoside chemistry, and [3+3] cyclisations.[84,85] One of latest is study of other members of deazapurine family – imidazo[4,5-*b*]pyridines and their corresponding N-nucleosides were studied by Ostrovskyi.[86,87]

My work is partly based on previous studies[88,89] of Dr. Iaroshenko and Prof. Dr. Groth. They have previously developed syntheses of several fluorinated purines, purine nucleosides and their mimetics**.**

The goal of current work is **design and synthesis of new potential drug-like scaffolds, i.e. polyfluorinated purine isosters bearing a 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one core.**

To achieve the goal of this work, next chapters are dedicated to the design and synthesis of novel 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one analogues bearing a variety of substituents at positions 1-, 2-, 4-, 5- and 6- in order to develop a library of compounds for biological evaluation.

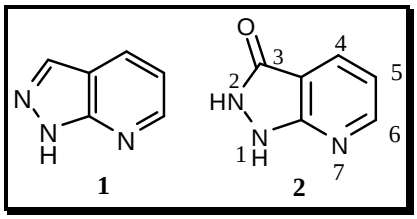
2. Results and discussions

2.1. Design and synthesis of novel deazapurine analogues bearing a 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one core

The subject of current part of this work is to develop a facile methodology for the preparation of novel compounds with potential biological activity bearing a 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one core.

2.1.1. Introduction

The 1*H*-pyrazolo[3,4-*b*]pyridine **1** framework is a key structural fragment of many heterocyclic compounds showing a broad spectrum of biological activity.[90-102]



1 **2**

Studies of the last decade show that heterocycles of this class possess antiviral[99a], anti-tumor[99b], anti-inflammatory[104], anti-microbial[105], and anti-parasitic properties.[106]

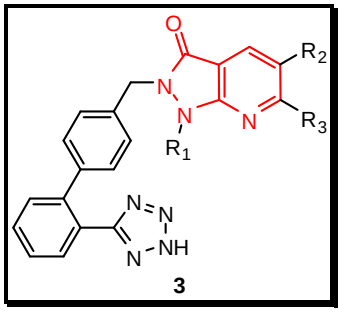
Fluorinated pyrazolo-[3,4-*b*]pyridines are also believed to be candidates for medications and considered to be potential inhibitors of ADA and IMPDH.[107] Primary attention has been given to the synthesis of CF_3-containing pyrazolo[3,4-*b*]pyridine.[97a]

The literature indicates different synthetic approaches to pyrazolo[3,4-*b*]pyridines. Condensation of the aminopyrazoles with α,β-unsaturated compounds is among them.[96b] Chanikov et al. recently synthesized a set of novel, fluoroalkyl-containing pyrazolo[3,4-*b*]pyridine derivatives which are considered as promising drug precursors.[108]

Similar to pyrazolo[3,4-*b*]pyridines, also 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2** can possess biological activity. It is known that the nitrogen atom at the position 7 of the purine framework plays an important role in the substrate/inhibitor recognition of the ADA enzyme family, since the amino acid asparagine forms a hydrogen bond with the nitrogen stabilizing the transition state of the adenosine deamination. Purine-like inhibitors which possess no nitrogen at position 7 are not recognized by the enzyme. This problem can be solved by

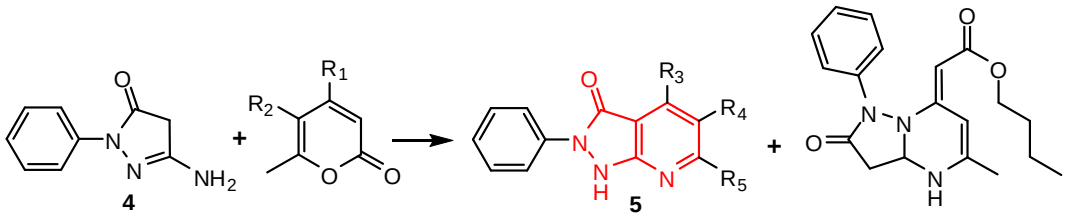
introducing small polar substituents located at a carbon atom, which are isosteric to the nitrogen atom (e. g., F, OH, O=, NH_2- and others capable for hydrogen bonding). Therefore, pyrazolo[3,4-*b*]pyridin-3-ones can serve as a core for novel, pharmacologically important purine isosteres.

Recently, few studies of compounds bearing core of pyrazolo[3,4-*b*]pyridin-3-ones appeared. Capelli *et al.* found that compounds **3** are promising cardiovascular system regulators.[109]



3

Group of Khouili recently published synthesis of **5** via condensation of 3-amino-1-phenylpyrazolin-5-one **4** with 2-pyrone derivatives.[110]



4 **5**

Scheme 3. Synthesis of pyrazolo[3,4-b]pyridin-3-ones.

2.1.2. Synthesis of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones

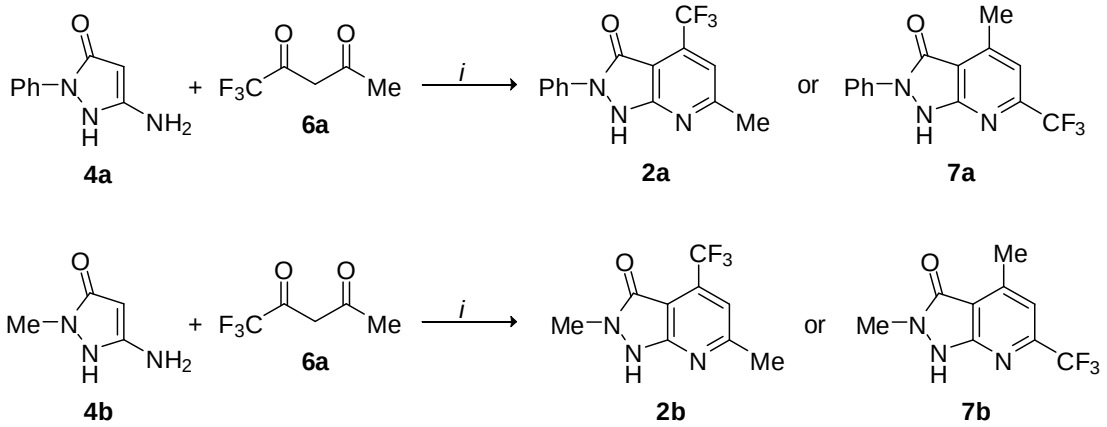
2.1.2.1. Reaction between 3-amino-1*H*-pyrazol-5(4*H*)-ones and 1,3-diketones

It has been reported that heteroannulation of electron-enriched heterocycles and bielectrophilic building blocks results in fused heterocyclic systems with the desired substitution pattern.[85,86] This concept has recently gained broad popularity of building up polyfluoro-substituted heterocyclic systems. It opens a wide range of practical routes towards fluorinated purine analogues and number of fluorine containing small heterocycles.

We decided to use 1-substituted 3-amino-1*H*-pyrazol-5(4*H*)-ones **4** and 1,3-diketones **6** as building blocks in order to obtain desired products. Compounds **4** are easily accessible in a

reaction of ethylcyanoacetate and corresponding hydrazine in the presence of sodium ethylate as described by Weissberger and Porter in 1940-ies.[112] Diketones **6** were purchased from chemical supply companies or synthesized using classical Claisen condensation.[113]

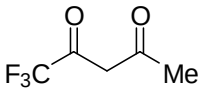
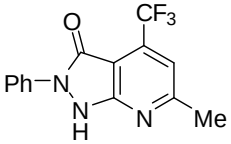
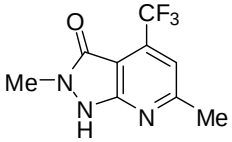
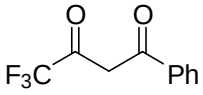
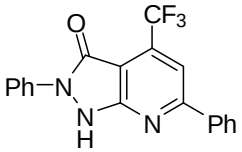
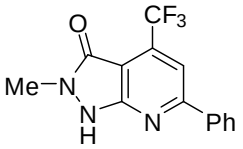
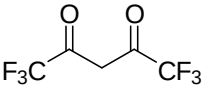
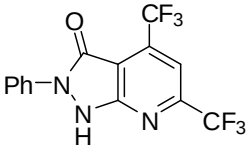
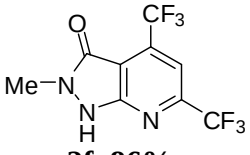
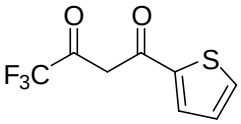
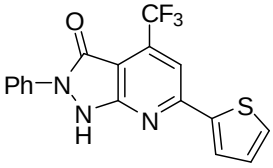
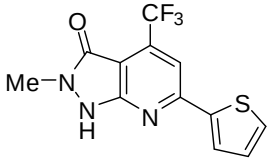
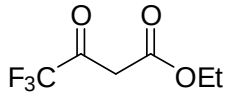
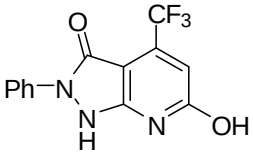
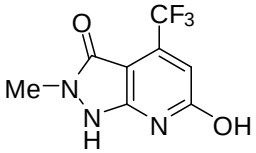
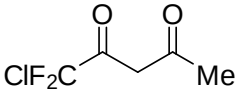
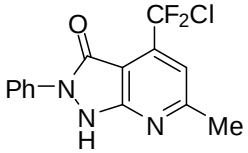
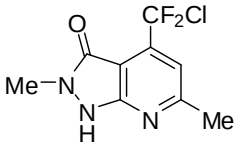
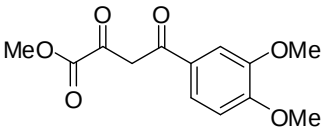
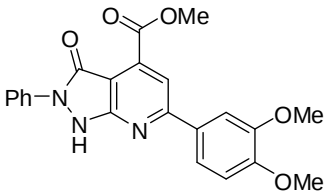
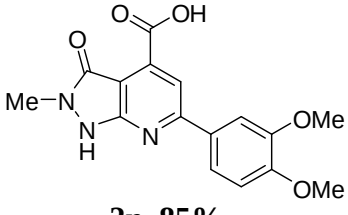
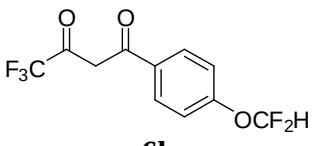
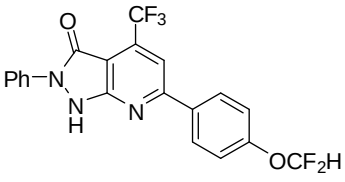
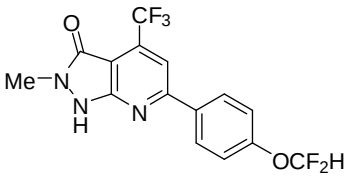
Under harsh conditions in relatively short time reaction between 3-amino-1-phenyl-1*H*-pyrazol-5(4*H*)-one **4a** and 1,1,1-trifluoropentane-2,4-dione **6a** resulted in desired product **2a** as a single stereoisomer. The same procedure was repeated but 1-methyl derivate **4b** instead of **4a** was employed, giving product **2b** in good yield (**Scheme 4**).

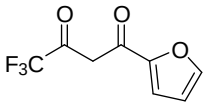
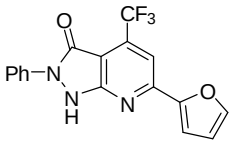
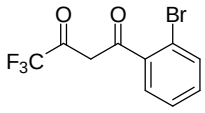
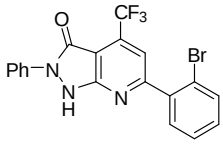
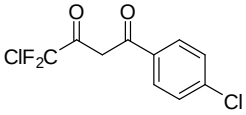
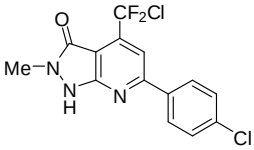
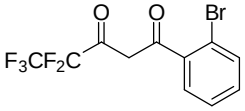
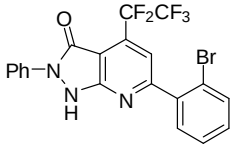
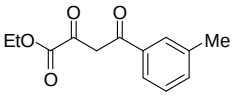
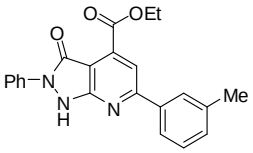
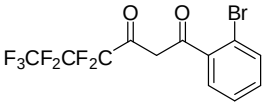
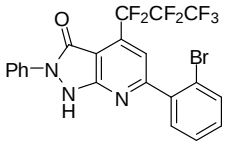
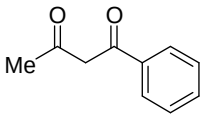
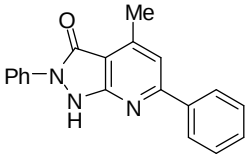
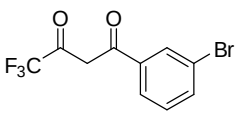
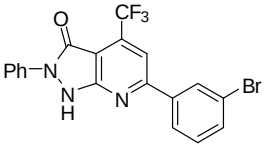
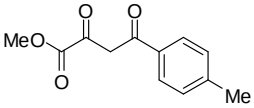
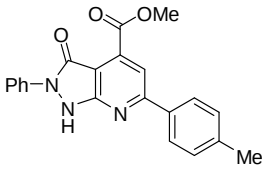
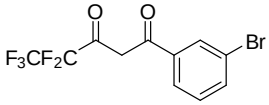
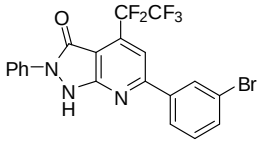
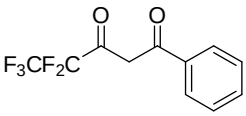
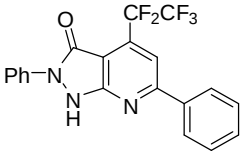
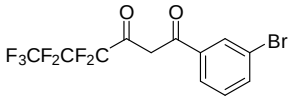
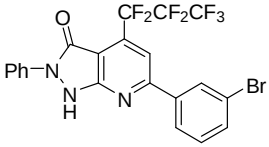
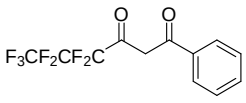
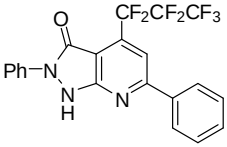
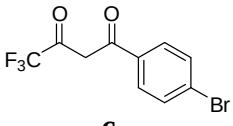
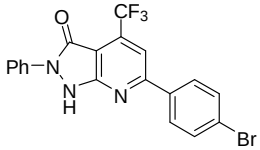


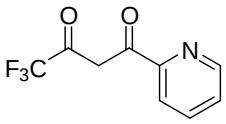
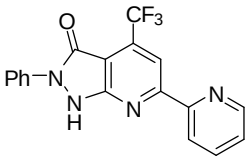
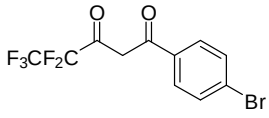
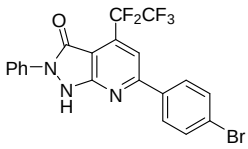
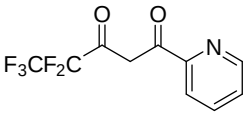
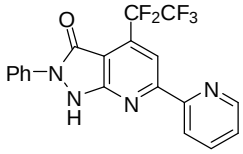
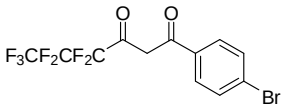
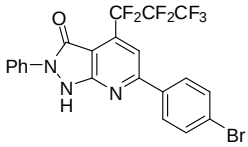
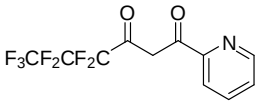
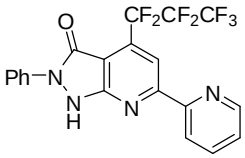
Scheme 4. Synthesis of **2a** and **2b**. *i* – AcOH; 118 ^{o}C, 2h.

Although two isomers **2** and **7** are possible, cyclocondensation showed excellent regioselectivity and only **2** was isolated. Likewise, reactions between 3-amino-1*H*-pyrazol-5(4*H*)-ones **4** and 1,3-diketones **6** resulted in 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2c-ai** as single isomers (**Table 1**).

Table 1. Synthesis and yields of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2a-ai**

	Yield (2)[a]	
 **6a**	 **2a, 82%**	 **2b, 63%**
 **6b**	 **2c, 98%**	 **2d, 74%**
 **6c**	 **2e, 89%**	 **2f, 86%**
 **6d**	 **2g, 81%**	 **2h, 99%**
 **6e**	 **2i, 52%**	 **2j, 77%**
 **6f**	 **2k, 64%**	 **2l, 74%**
 **6g**	 **2m, 70%**	 **2n, 85%**
 **6h**	 **2o, 69%**	 **2p, 99%**

	Yield (2)[a]		Yield (2)[a]
 **6i**	 **2q, 89%**	 **6s**	 **2aa, 91%**
 **6j**	 **2r, 96%**	 **6t**	 **2ab, 88%**
 **6k**	 **2s, 65%**	 **6u**	 **2ac, 79%**
 **6l**	 **2t, 69%**	 **6v**	 **2ad, 97%**
 **6m**	 **2u, 80%**	 **6w**	 **2ae, 91%**
 **6n**	 **2v, 81%**	 **6x**	 **2af, 94%**
 **6o**	 **2w, 76%**	 **6y**	 **2ag, 79%**

	Yield (2)[a]		Yield (2)[a]
 **6p**	 **2x, 92%**	 **6z**	 **2ah, 80%**
 **6q**	 **2y, 95%**	 **6aa**	 **2ai, 85%**
 **6r**	 **2z, 97%**		

[a] – yields refer to pure isolated products

New synthesized 1*H*-pyrazolo[3,4-*b*]pyridin-3-ones **2** are crystalline compounds, often with high melting points. Colours, depending on substitutes, change from white to yellow to black. The structures of all compounds **2** were characterized by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis. Many of synthesized pyrazolo[3,4-*b*]pyridin-3-ones, especially 2-methyl derivatives are low soluble in most popular solvents even at high temperature and they tend to crystallize as long needles. Therefore in some cases characterization of compounds using NMR spectroscopy failed, especially ^{13}C NMR spectral analysis, which requires high concentration of analyte because of high substitution rate. However, even when the compound is more soluble, polyfluoroalkyl groups, if present, appear as undecipherable multiplets. The presence of fluorinated alkyl groups was confirmed by ^{19}F NMR and, indirectly by spectral analysis of previously synthesized diketones. Those are highly soluble compounds and because of hydrogen close to polyfluoroalkyl group, ^{13}C spectral signals of the latter are intensive enough to see exact multiplicity even in case of n-C_3F_7.

^{19}F NMR analysis helped to determine position of perfluoroalkyl group in pyrazolo[3,4-*b*]pyridin-3-ones. It was helpful especially in case if **2** was bearing CF_3 group. All CF_3 group

containing products were compared to **2e** and **2f**. Bearing two CF_3 groups which appear in ^{19}NMR spectra at positions -61 ppm (4-CF_3) and -67 ppm (6-CF_3), both are excellent symmetric model compounds. Nitrogen at position 7 shifts the signal of 6-CF_3 to lower field causing a small but notable difference. Since other CF_3 containing pyrazolo[3,4-*b*]pyridin-3-ones show a signal at around -61, there is no doubt that trifluoromethyl group is placed at position C4.

The structure of **2g** was independently confirmed by X-ray analysis (**Figure 6**).

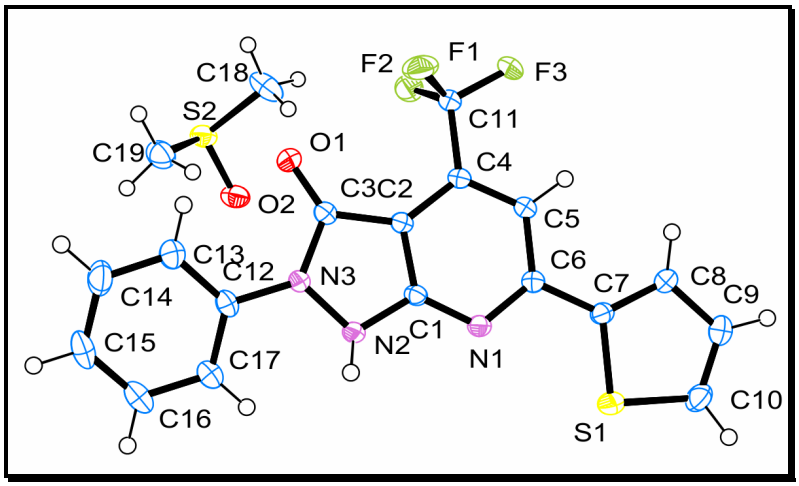
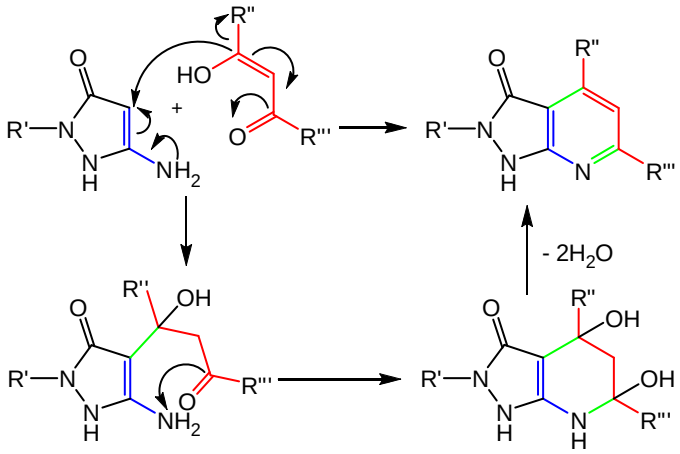


Figure 6. Ortep plot of 2-phenyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **2g**. Crystal solvate with DMSO.

The fact that only one stereoisomere **2** was isolated is explained by reaction mechanism, outlined in **Scheme 5**. Most electron-deficient carbon of 1,3-diketone, which exists in its enol form, according to ^{1}H NMR spectra of synthesized diketones, attacks to most electron-rich position of **4**, forming Michael adduct, which undergoes intramolecular cyclisation and, with water elimination, aromatization. Thus, the more electron-rich substituent will always be at the position C4 of the molecule of **2**.



Scheme 5. Mechanism of formation of 1*H*-pyrazolo[3,4-*b*]pyridin-3-ones **2**.

2.1.2.2. Modification of pyrazolo[3,4-*b*]pyridin-3-ones via carbon-carbon coupling reactions

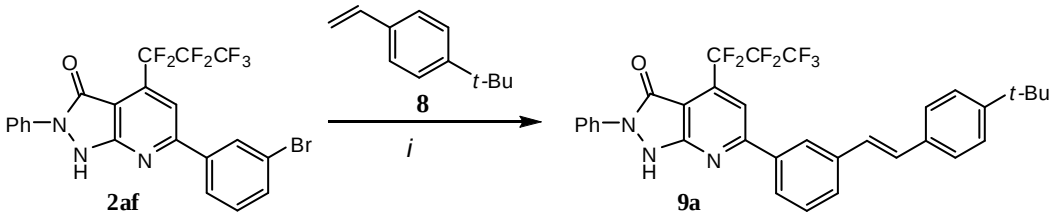
Bromine-containing pyrazolo[3,4-*b*]pyridin-3-ones **2aa-ai** were prepared with a particular goal – to expand structural diversity via palladium-catalyzed carbon-carbon (C-C) coupling reactions[114] namely the Suzuki-Miyaura coupling,[115] the Heck[116] and the Sonogashira[117] reaction. These are probably the most important C-C coupling reactions; they are catalyzed by palladium and have been abundantly used in syntheses and widely studied in recent decades.

The father of palladium-catalysed coupling chemistry is generally considered to be Professor Richard Heck. Although first discovered by Mizoroki, it was through work of Heck in the early 1970s that the Pd-catalysed reactions became widely known and applied.[118] The Heck reaction is broadly defined as the palladium-catalyzed coupling of alkenyl or aryl (sp^2) halides or triflates with alkenes to yield products which formally result from the substitution of a hydrogen atom in the alkene coupling partner. Heck reaction is considered as best evolved, including a multitude of asymmetric variants.

Seeking for the best conditions for all three reactions was based on principal similarities of our substrates with successful examples published. In quest of best conditions the low solubility of substrate had to be taken in mind.

Heck reaction was the first to perform. Just few trials helped to find optimal conditions for Heck reaction: synthesis of **9a** was performed in a pressure tube, under inert atmosphere. 1 Equivalent of 6-(3-bromophenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **2af**, 3 equivalents of 4-*tert*-buthylstyrene **8**, 4 equivalents of triethylamine, catalyst

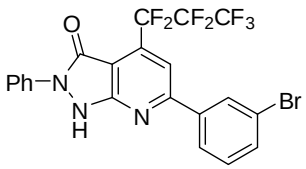
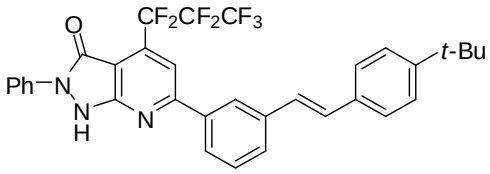
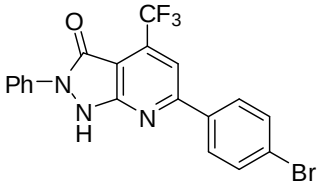
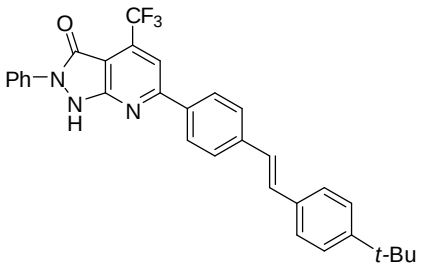
$PdCl_2(PPh_3)_2$ (4mol%) and dry DMF as solvent were used. Reaction resulted in expected product **9a** (**Scheme 6**).

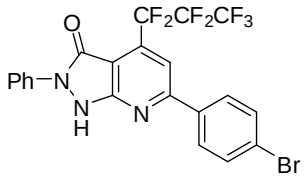
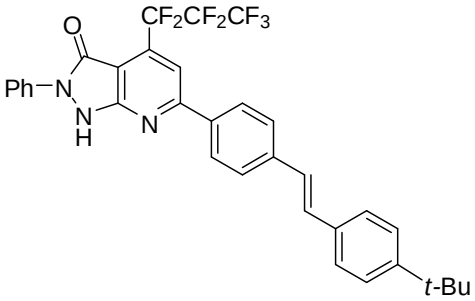


Scheme 6. Heck coupling between **2af** and 4-*t*-buthylstyrene. *i* – TEA, 4eq; $PdCl_2(PPh_3)_2$, 4mol%; DMF, 140 ^oC, 8h.

Same protocol was applied in other reactions between pyrazolo[3,4-*b*]pyridin-3-ones **2** and 4-*tert*-buthylstyrene **8** (**Table 2**). Reactions of 3-bromophenyl and 4-bromophenyl derivatives resulted in desired products which were afforded in good yields. The situation was different when 2-bromophenyl derivatives were used - after repeated trials only starting material was isolated. Most probably, Br atom is too sterically hindered to enter the reaction.

Table 2. Synthesis and yields of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **9a-c**

	Yield (9)[a]
 **2af**	 **9a, 77%**
 **2ag**	 **9b, 81%**

	Yield (9)[a]
 **2ai**	 **9c, 84%**

[a] – yields refer to pure isolated products

All synthesized compounds were characterized by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis. Similar to their precursors, also the products **9** are poorly soluble thus burdening spectral analysis. An attempt to grow a crystal was partially successful – a crystal of **9b** was obtained which gave proof of structure (**Figure 7**). However, the quality of the crystal was too low to obtain precise crystal parameters.

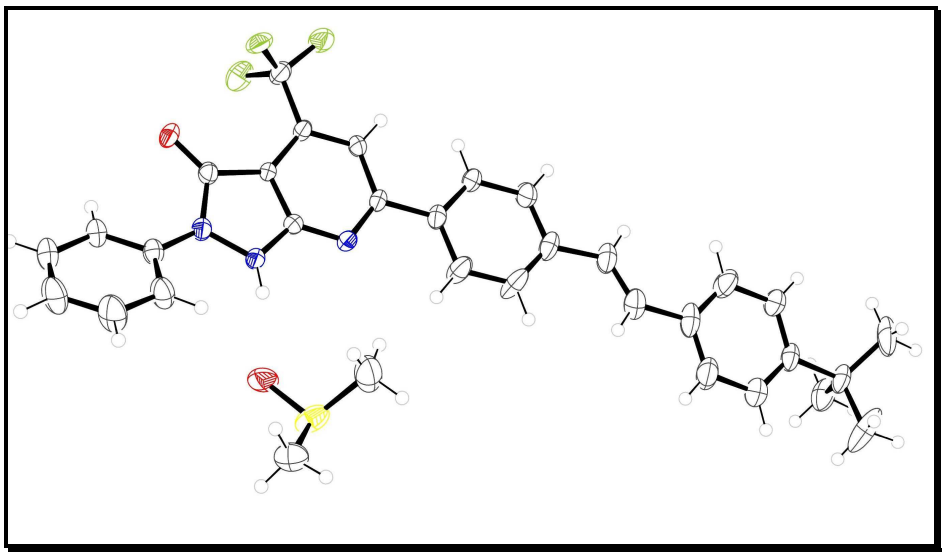
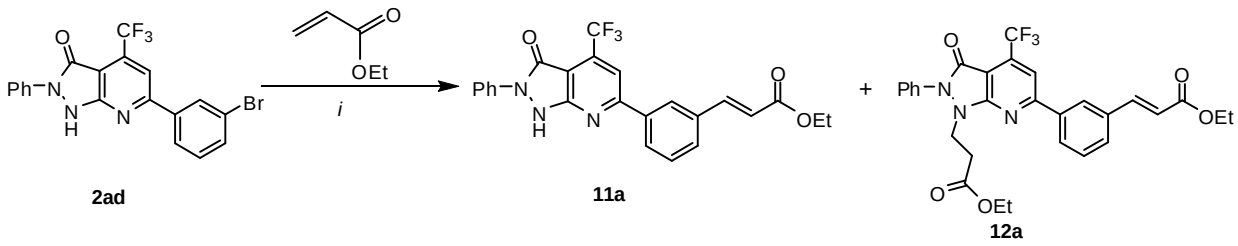


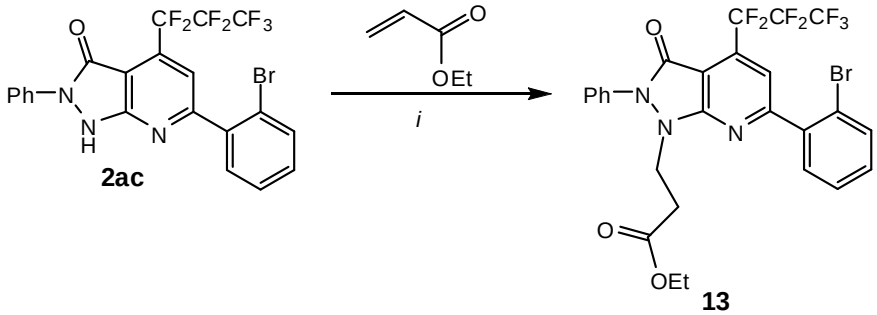
Figure 7. Crystal structure of **9b** (crystal solvate with DMSO).

Contended with successful results, we decided to try reactivity of alkenes bearing electron-withdrawing group. Ethylacrylate **10** was considered as attractive reagent. Similar conditions as in synthesis of **9** were used here. In contrast with the latter, reaction of **2ad** with ethylacrylate went an unexpected pathway. Besides Heck coupling, another process – Michael addition of ethylacrylate at position N1 – took place simultaneously giving a mixture of two products – **11a** and **12a** (**Scheme 7**).



Scheme 7. Heck coupling between **2ad** and ethylacrylate. *i* – TEA, 4eq; $PdCl_2(PPh_3)_2$, 4mol%; DMF, 100 ^oC, 20h.

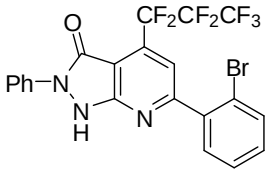
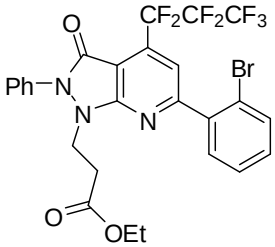
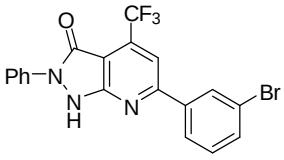
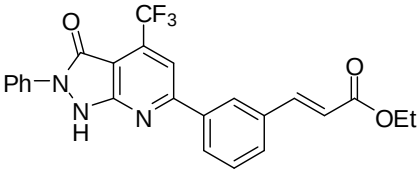
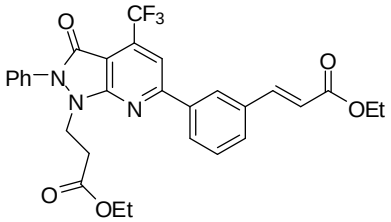
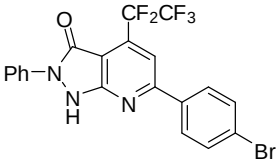
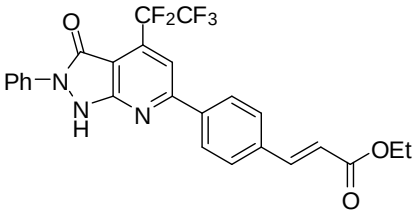
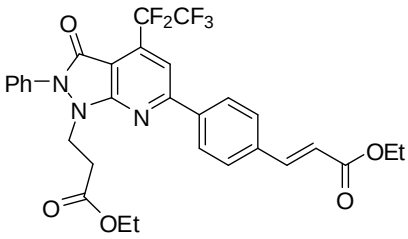
Likwise, reaction between other brominated pyrazolo[3,4-*b*]pyridin-3-ones **2** and ethylacrylate was performed. Again, *ortho*-Br in **2ac** proved to be too sterically hindered to enter the reaction; only Michael addition occurred giving product **13** (**Scheme 8**).



Scheme 8. Reaction between **2ac** and ethylacrylate. *i* – TEA, 4eq; $PdCl_2(PPh_3)_2$, 4mol%; DMF, 100 ^oC, 12h.

Reaction products and yields are summarized in **Table 3**.

Table 3. Synthesis and yields of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **11-13**.

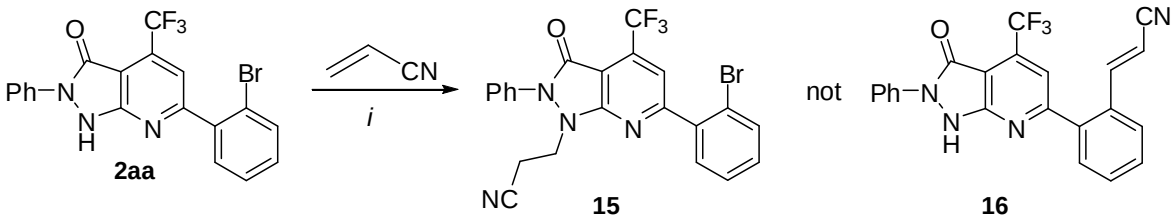
	Products and yields[a]	
 **2ac**	 **13, 70%**	
 **2ad**	 **11a, 42%**	 **12a, 18%**
 **2ah**	 **11b, 34%**	 **12b, 24%**

[a] – yields refer to pure isolated products

In order to obtain higher yields of desired product **11**, several optimizations were performed – 1.2 eq of ethylacrylate instead of 3eq were used, also reaction time and temperature was modified. Although by decreasing the amount of ethylacrylate, reaction time and temperature, higher yields of desired product **11** could be isolated, the formation of side product **12** was unavoidable. Reaction at N1 is possible because of the basic effect of TEA – an anion at N1 is formed, which is followed by attack of ethylacrylate via Michael addition. The most convenient way to desired product **11** would be introduction of appropriate *N*-protecting group and subsequent deprotection after Heck reaction has taken place. The protecting group

has to be easily removable, but at the same time it has to be stable during Heck reaction. This means looking for possibly mildest conditions since many amine protecting groups are easily cleaved when heated or treated with acid or base. Possible choices would be *p*-toluenesulfonic (tosyl-) or benzyl-groups, since they are stable in highly basic media in high temperatures.[119] Structures of **11 – 13** were confirmed by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis.

Similar to ethylacrylate, acrylonitrile was introduced in the reaction. Again, Br in *ortho*-position proves to be unreactive – instead of Heck reaction different process took place and N1 Michael adduct **15** instead of expected product **16** formed (**Scheme 9**).



Scheme 9. Reaction of **2aa** with acrylonitrile. *i* – TEA, 4eq; $PdCl_2(PPh_3)_2$, 4mol %; DMF, 90 ^{o}C, 24h.

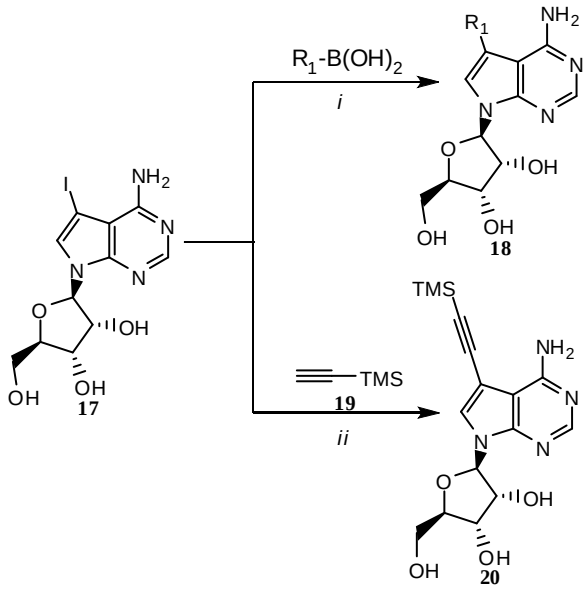
Structure of **15** was confirmed by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis. The main evidence of direction the reaction took is two triplets (2 protons each) in ^{1}H NMR spectra; two signals indicating CH_2 in DEPT spectra and doublets in mass spectra proving the presence of Br.

Unfortunately, because of limited time further reactions with acrylonitrile were not performed but it is most probable that if Br atom is located at *meta*- or *para*- positions, two processes – Heck and Michael addition – would occur simultaneously, and an appropriate protecting group of nitrogen would lead the reaction in desired way.

Although reactions of **2** with ethylacrylate and acrylonitrile did not go entirely the desired path, the products **12**, **13** and **15** still have potential to be biologically active substances. Both propanenitrile and ethylpropanoate groups can be referred to as acyclic sugar analogues. Besides they can be employed in several reactions giving new kinds of products.

Unsuccessful experiments

After countless trials we had to admit that Suzuki-Miyaura and Sonogashira reactions do not give satisfactory results. In Sonogashira reactions, complete conversion of starting materials was observed, but TLC showed that mixture of highly polar compounds was formed and separation by column chromotagrophy was impossible. To the contrary, in Suzuki-Miyaura reaction only starting material was isolated; the main reason for the failure is the low solubility of substrate or inorganic base. Clearly, different approach must be used. Recently, the synthesis of tubercidine analogues with anti-cancer activity was patented[120] where target compounds were afforded from 7-iodotubercidine **17** via Suzuki-Miyaura and Sonogashira reactions. Suzuki-Miyaura cross coupling reactions of 7-iodotubericidine with corresponding aryl and hetaryl boronic acids were performed under aqueous conditions,[121] while ethynyl derivative **20** was prepared by Sonogashira reaction of **17** with trimethylsilylacetylene **19**.



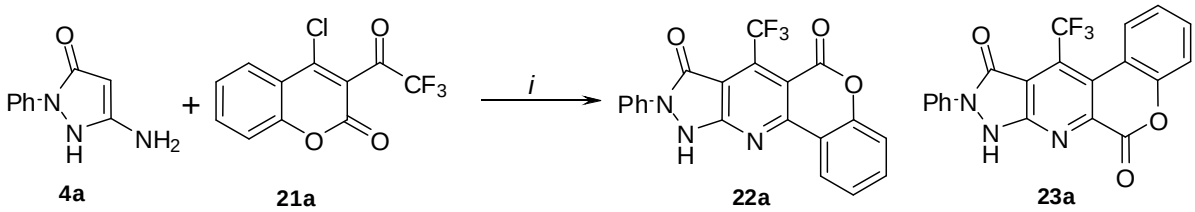
Scheme 10. Cross-coupling reactions of 7-iodotubercidine described in literature.Reagents and conditions: *i* – $Pd(OAc)_2$, TPPTS, Na_2CO_3, CH_3CN/H_2O, 80 ^oC, 1h; *ii* – $PdCl_2(PPh_3)_2$, TEA, DMF, RT, 16h.

This strategy would be convenient also in my current work. Nucleosides are more soluble than their corresponding aglykones, and position N1 is protected thus avoiding unwanted reaction path. Probably, it would be possible to perform also Heck reaction without need to seek for appropriate *N*-protecting group.

2.1.3. Synthesis of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones

Being interested in the development of new methods of pyrazolo[3,4-*b*]pyridin-3-one construction, we considered coumarine scaffolds as building blocks in cyclocondesation reactions with 1-substituted 3-amino-1*H*-pyrazol-5(4*H*)-ones. The latter are formally condensed enamines, and therefore could be considered as useful binucleophiles.

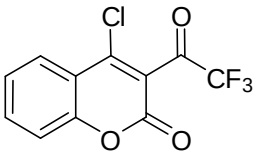
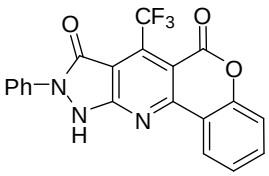
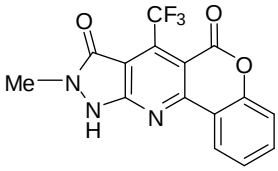
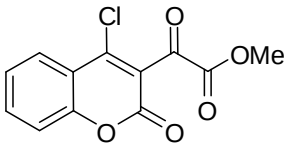
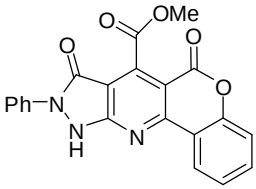
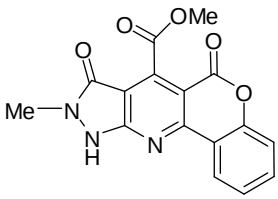
We decided to use 3-acyl-4-chlorocoumarines which were afforded from commercially available 4-hydroxycoumarine in one pot synthesis developed recently by the group of Langer.[122] Since 3-acyl-4-chlorocoumarines **21** proved to be sensitive to moisture, reaction between 5-aminopyrazolone **4a** and **21a** was performed in a pressure tube under inert atmosphere; dry DMF was used as solvent and TMSCl as water scavenger (**Scheme 11**). Trying different reaction temperatures (RT to 120 ^{o}C) and reaction times (up to 12 h), we found that dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-dione **22a** can be afforded in good yield when heated at 83 ^{o}C for 3h.
Although two isomers **22a** and **23a** are possible, the cyclocondensation showed excellent regioselectivity and only one stereoisomere **22a** was observed and isolated.



Scheme 11. Synthesis of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-dione **22a**. *i* – TMSCl, DMF, 83 ^{o}C, 3h.

The same protocol was applied in synthesis of other dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones **22b-d**. Like in first synthesis, formation of reaction product **22** instead of **23** was observed.

Table 4. Synthesis and yields of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones **22a-d**

	Yield (2)[a]	
 **21a**	 **22a, 65%**	 **22b, 57%**
 **21b**	 **22c, 60%**	 **22d, 68%**

[a] – yields refer to pure isolated products

Products **22** are crystalline compounds with high melting points. Yields of isolated cycloadducts are reduced because of instability of 3-acyl-4-chlorocoumarines **21**. An evidence of side-reactions and degradation of starting materials was the intensive black color of reaction mixture and observation of highly polar compounds on TLC.

The structures of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones **22** were characterized by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis. ^{19}F NMR was used to prove the presence of CF_3 group for **22a** and **22b**. Unfortunately, low solubility in most popular solvents made characterization of **22b** and **22d** by NMR spectroscopy difficult.

The main proof for the structure of **22** is based on ^{13}C NMR spectra. Studies of theoretically estimated ^{13}C NMR spectra show only one notable difference (**Figure 8**). The atom C6a (marked with red) theoretically appears at 122 ppm in case if **22** is formed, while in case of **23** the same atom would appear at 138 ppm. All experimentally measured ^{13}C NMR spectra show a signal at 118 ppm which is clear evidence towards structure **22**. 2D NMR measurements of **22a** show correlation between CCF_3 and carbonyl group.

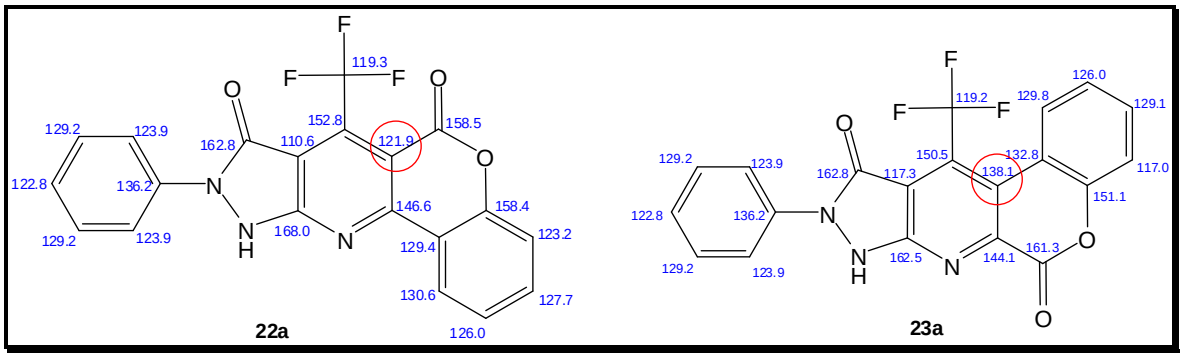
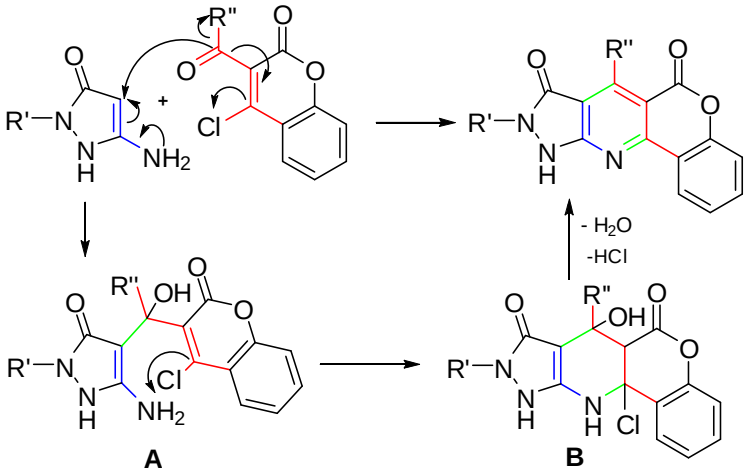


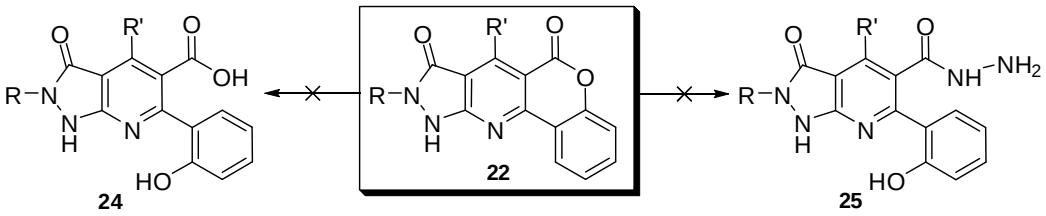
Figure 8. Estimated ^{13}C NMR signals of **22a** and **23a**.

Proposed mechanism involves Michael addition of α,γ-dielectrophile to heterocycle leading to intermediate **A**, which undergoes intramolecular cyclisation to **B** and, with subsequent water elimination, formation of **22** (**Scheme 12**).



Scheme 12. Mechanism of formation of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones **22**.

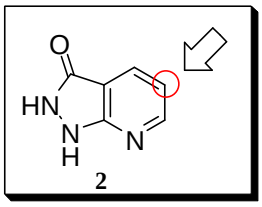
We tried opening the pyrone ring using KOH in MeOH or hydrazine hydrate (**Scheme 13**). Significant, in both cases, addition of base resulted in immediate color change of yellow solution to dark red mixture. Unfortunately, both methods gave an unseparatable mixture of highly polar compounds.



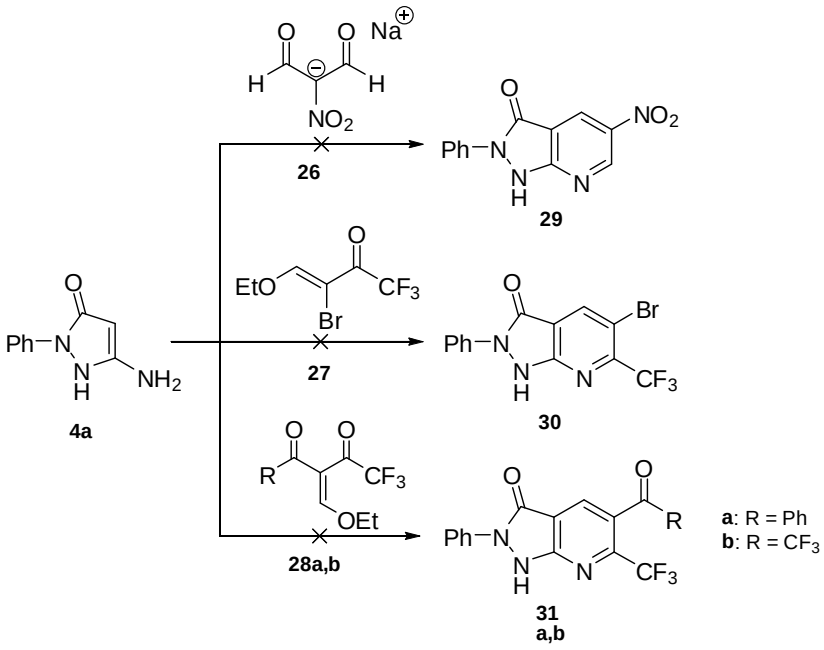
Scheme 13. Unsuccessful ring-opening reactions of **22**.

2.1.4. Synthesis of 5-substituted pyrazolo[3,4-*b*]pyridin-3-ones

Next, we decided to modify the pyrazolo[3,4-*b*]pyridin-3-one **2** system by introducing a substituent at position C5 which was unsubstituted in all previously synthesized pyrazolo[3,4-*b*]pyridin-3-ones.

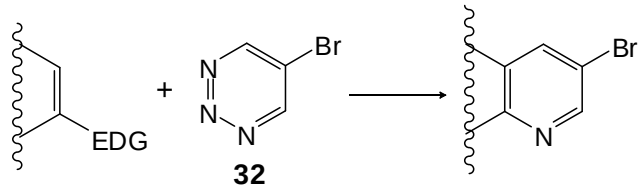


We considered an introduction of different functionalities using several dielectropfiles **26 – 28** (**Scheme 14**), but all attempts to find appropriate conditions and isolate desired products failed – unseparatable mixture of highly polar compounds formed.



Scheme 14. Unsuccessful trials to form 5-substituted pyrazolo[3,4-*b*]pyridin-3-ones.

Therefore, a different strategy to obtain 5-substituted pyrazolo[3,4-*b*]pyridin-3-ones had to be found. A recent study[123] of the reactivity of 5-bromo-1,2,3-triazine **32** catched our attention. It is well known fact that inverse electron demand Diels-Alder (DA_{Inv}) reactions of electron-deficient heterocyclic azadienes have been used as powerful cycloaddition reactions central to a series of natural product total syntheses whose structures possess highly functionalized heterocyclic ring systems not easily accessed by conventional methods.[124] Several studies have demonstrated the ability of 1,2,3-triazines to participate in inverse electron demand Diels-Alder reactions, typically with enamine[125] and ynamine[126] dienophiles. Br atom as C5 substituent converts 1,2,3-triazine into a heterocyclic azadiene system with a reaction scope that portends extensive synthetic utility, substantially expanding the range of participating dienophiles.[123]



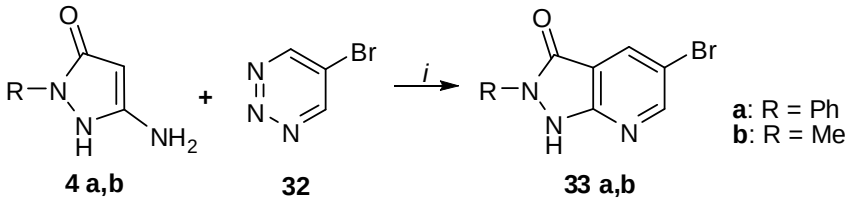
Scheme 15. Inverse electron demand Diels-Alder (DA_{Inv}) reaction of 1,2,3-triazine.

Therefore we decided to use 5-bromo-1,2,3-triazine **32** to bring a Br atom into C-5 position thus opening a scope for further reactions namely Suzuki-Miyaura, Sonogashira and Heck.

The synthesis of **32** was performed according to a known method[127] using 4-bromopyrazole and hydroxylamine-O-sulfonic acid with subsequent oxidative ring expansion by treatment with $NaIO_4$. 4-Bromopyrazole was synthesized in excellent yield in a reaction of unsubstituted pyrazole with N-bromosuccinimide in CCl_4.[128]

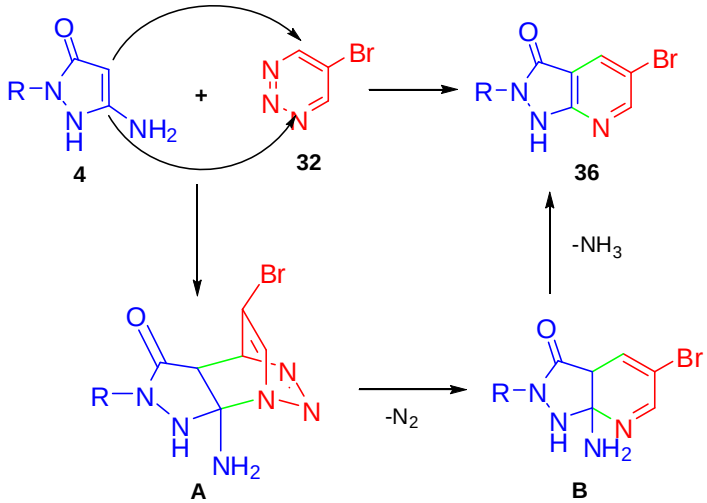
Next, we conducted a trial experiment by stirring a mixture of 5-bromo-1,2,3-triazine **32** and 3-amino-1-phenyl-1*H*-pyrazol-5(4*H*)-one **4a** in acetic acid at RT overnight. A small amount of brown solid was isolated which, according to ^{1}H NMR spectra, proved to be the desired product **33a**. The yield of less than 20% is explained with instability of bromotriazine under acidic conditions. Therefore isopropanol was used as solvent and during stirring a reaction mixture under reflux for 2 hours, formation of product as brown precipitation was observed. Filtration and washing with hot ethanol gave 96% yield of desired 5-bromo-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **33a** (**Scheme 16**). To our disappointment, product showed limited solubility in all popular solvents thus limiting the scope of further applications. As

expected, use of 3-amino-1-methyl-1*H*-pyrazol-5(4*H*)-one **4b** gave a quantitative yield of insoluble pyrazolo[3,4-*b*]pyridine-3-one **33b**.



Scheme 16. Synthesis of 5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **33**.

As indicated before, the reaction between 1,2,3-triazine and electron-rich heterocycles is classified as an inverse electron demand Diels-Alder reaction. Intermediate **A** is formed by attack of dienophile **4** on diene **32**, subsequent elimination of N_2 leads to intermediate **B**, which turns into target product **33** by elimination of NH_3 (**Scheme 17**).



Scheme 17. Mechanism of formation of 5-bromo-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **33**.

The fact that pyrazolo[3,4-*b*]pyridine-3-ones **33** are insoluble in most solvents, makes the use of these compounds as substrates for further syntheses difficult. Attempts to perform Suzuki-Miyaura coupling failed completely since we could not find a solvent to dissolve the substrates.

2.1.5. Conclusions

In conclusion of this chapter, a set of 51 by far unknown deazapurine analogues is synthesized. Bearing a strong-withdrawing group these compounds are potential inhibitors of ADA and IMPDH, and can show a broad variety of biological activities. For example, (*E*)-6-(4-(4-tert-butylstyryl)phenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **9b** can be potential liquid crystal, since it is a long, thin molecule with a relatively low melting point.

Most target substances are obtained in moderate to excellent yields using classical approach involving [3+3] cyclocondesation of enamine fragment-containing heterocycle – aminopyrazolone – and bielectrophiles – 1,3-diketones or 3-acyl-4-chlorocoumarines. Inverse demand Diels-Alder reaction was applied for synthesis of 5-substituted pyrazolo[3,4-*b*]pyridin-3-ones. Modification of bromine-containing pyrazolo[3,4-*b*]pyridin-3-ones was performed using Pd-catalyzed reactions.

2.2. Design and synthesis of novel deazapurine glycosides as potential inhibitors of adenosine deaminase and inosine-5′-monophosphate dehydrogenase

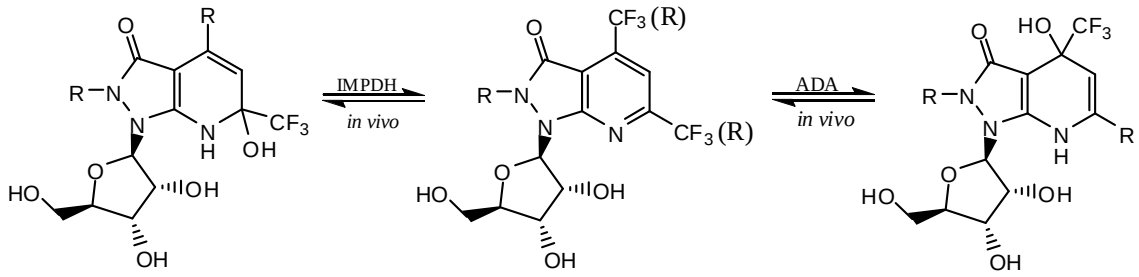
Present part of this work is focused on synthesis of glycosides and their analogues, employing a selection of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones described in previous chapter.

2.2.1. Introduction

As it was indicated before, nucleosides, especially fluorinated derivatives, have found widespread applications in chemistry, physics, and biology. Our subject of interest, inhibition of ADA and IMPHD, is listed among them.

The key step of inosine formation via ADA-catalyzed deamination is the nucleophilic addition of water to position 6 of the adenine fragment.[129] A study of Lindell *et al*, which was based on calculations of the enthalpy of covalent hydration of a number of different nucleosides, proved that a stronger electron-withdrawing character of the aglycone facilitates the hydration process by increasing the absolute value of enthalpy.[130, 131]

To inhibit an enzyme, it is obligatory to match the requirements of the targeted binding pocket. The sterical similarity of the trifluoromethyl and the amino group, in combination with the highly withdrawing character of the CF_3 residue, makes 4- or 6-trifluoromethyl-substituted 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones interesting substrates for studies of ADA or IMPHD inhibition.



Scheme 18. Possible interraction of target molecules with ADA and IMPDH.

Similar to the CF_3 group, the presence of the polyfluorinated group can facilitate the addition of a water molecule and the formed hydrate will coordinate on the ADA's cofactor zinc moiety with OH function leading to the enzyme inhibition. It is also known that the fluorine atoms of perfluoroalkanes show affinity to Lewis acidic metal cations,[31c, 132] such as Li^+, Al^{3+}, Ga^{3+}, Mg^{2+}, and Zn^{2+}. Since the active site of ADA-type inhibitors possesses an incorporated zinc cation, it could be advantageous to introduce perfluoroalkyl groups in the inhibitor. The Rf groups would interact with the metal cation and result in the formation of a stable associate and enzyme inactivation. Besides, it is been reported that polyfluoro group, incorporated in nucleoside, increases bioavailability of the molecule.[83]

2.2.2. Synthesis of N-nucleosides of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones

The advantages of CF_3 and polyfluoroalkyl groups listed previously directed us into design of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2** described in previous chapter. Now, motivated by biological importance of nucleosides, we decided to transform both fluorinated and non-fluorinated pyrazolo[3,4-*b*]pyridin-3-ones into potentially useful nucleosides and their analogues.

There are different applicable approaches to the synthesis of a variety of nucleosides. Theoretically they can be classified into four categories based on the strategies they use:

1) Construction of an aglycone unit upon a carbohydrate moiety;
2) Construction of a carbohydrate moiety upon an aglycone unit;
3) Direct coupling of a carbohydrate moiety with a preformed aglycone unit;
4) Modification of the existing N-nucleosides.

Since we have synthesized a variety of N-deprotected deazapurine analogues, direct coupling with a carbohydrate moiety is most convenient way to achieve N-nucleosides. Following work done by us includes synthesis of both cyclic nucleosides and molecules which could be referred as acyclic analogues of nucleosides.

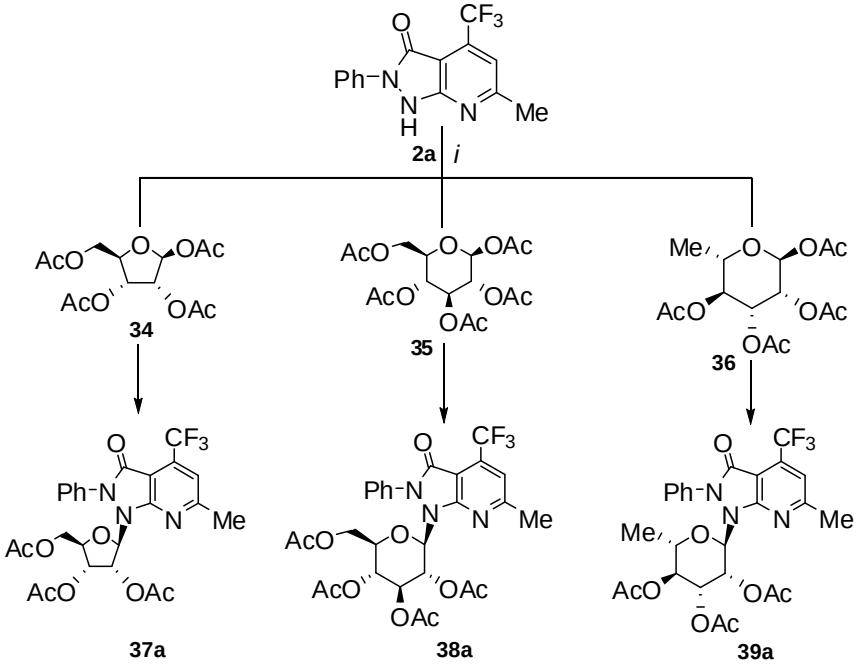
2.2.2.1. Cyclic nucleosides

As mentioned above, we decided to attach carbohydrate moiety directly to our heterocycles. After studying a number of glycosilations most suitable method was selected. The so-called silyl Hilbert-Jones method[133] is based on a preliminary activation of heterocyclic moiety with

N,O-bis(trimethylsilyl)acetamide (BSA), resulting in generation of N-silylated intermediate, which reacts with peracylated sugar in presence of weak Lewis acid, such as TMSOTf. Following this method, Dr. Ostrowski from our group successfuly synthesized a handful of nucleosides.[86, 87]

Three peracetylated carbohydrates were chosen - 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose **34**, 1,2,3,4,6-penta-O-acetyl-β-D-glucose **35** and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose **36**. The choice of above mentioned sugars was based on fact that all of them are components of naturally occurring nucleosides and, in fact, α-L-rhamnose is one of only three naturally occurring α-sugars.

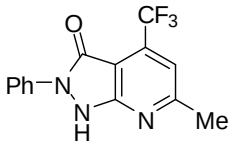
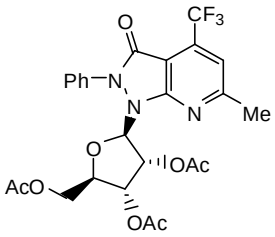
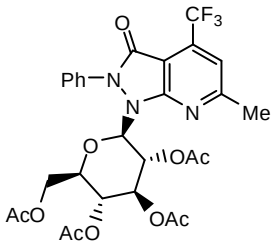
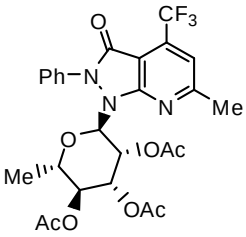
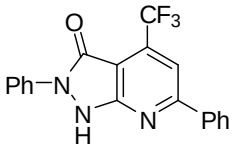
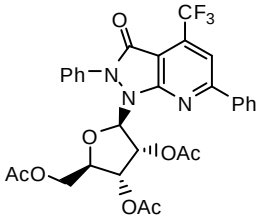
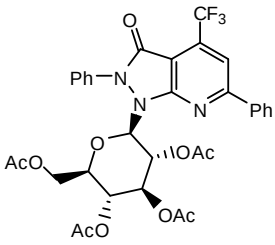
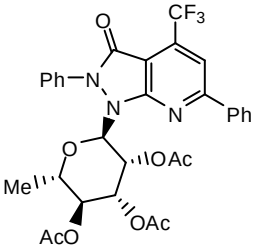
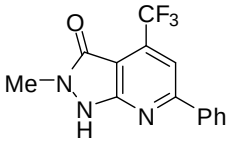
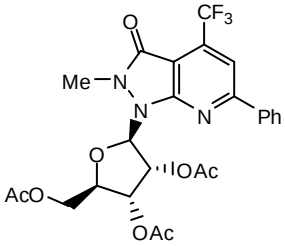
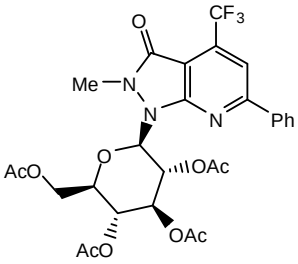
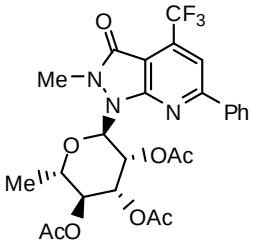
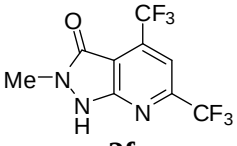
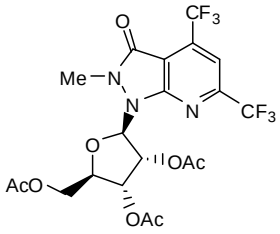
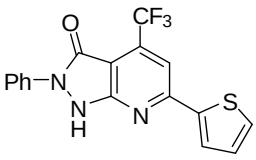
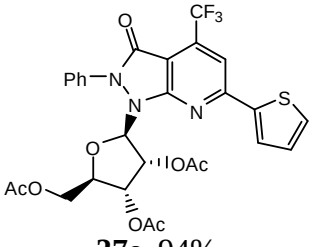
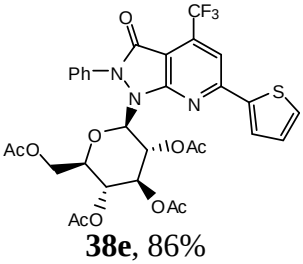
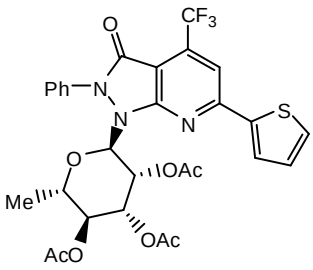
In the first step of reaction, 1.1 equiv. of BSA was added to a suspension of **2a** in dry acetonitrile and the mixture was heated at reflux for 20 minutes, during this time a clear solution was formed - this indicates the successful initial silylation. In the next step, without isolation of intermediate, a solution of 1.1 equiv. of acetylated sugar in CH_3CN and catalytic amount of TMSOTf (25 mol%) was added and refluxing continued (**Scheme 19**). The progress was monitored with TLC. After refluxing for 2 hours, conversion of most of pyrazolo[3,4-*b*]pyridinone **2a** was observed. To attain complete conversion, heating was prolonged up to 12 hours but, as it was observed by TLC, continuous decomposition of product takes place. Therefore, reaction time was limited to 2 hours.

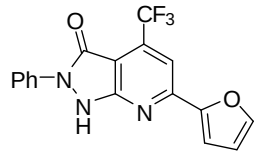
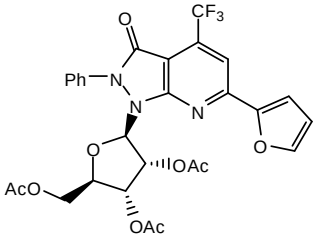
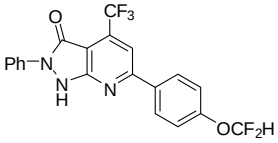
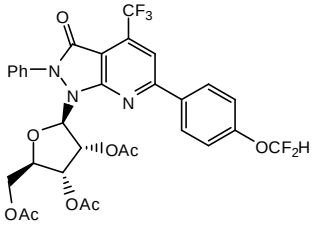
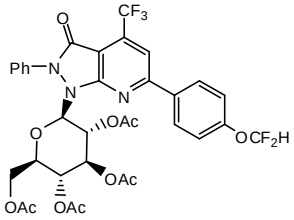
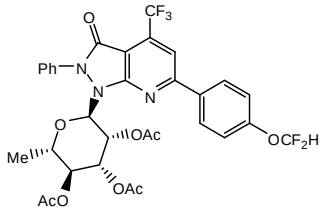
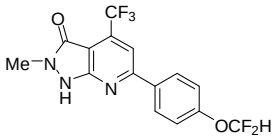
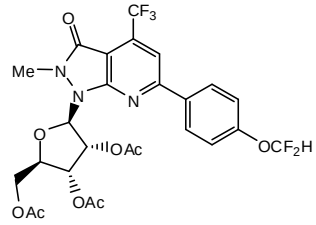
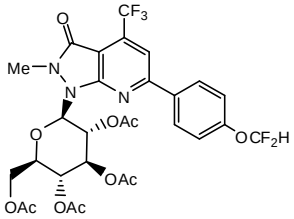
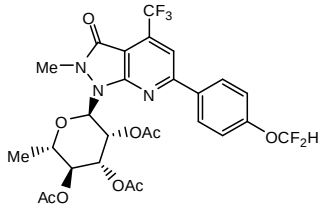
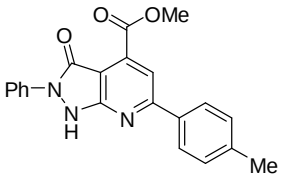
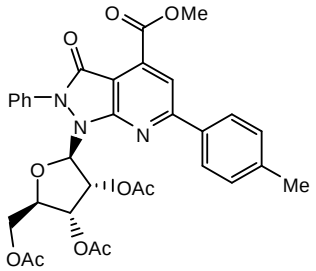
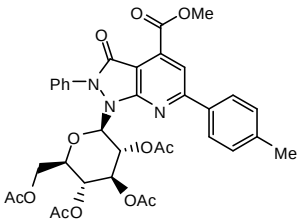
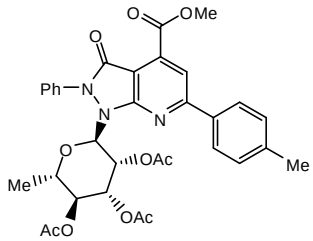
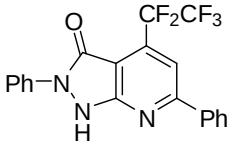
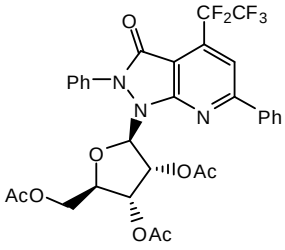
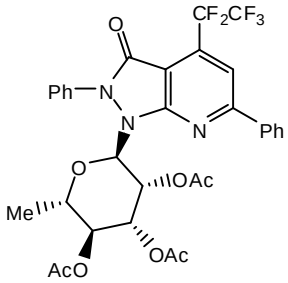
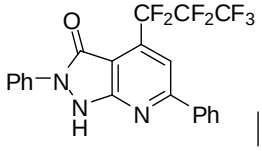
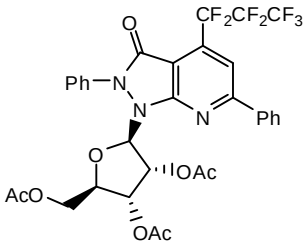


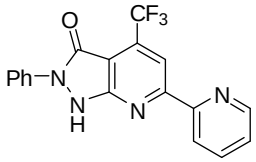
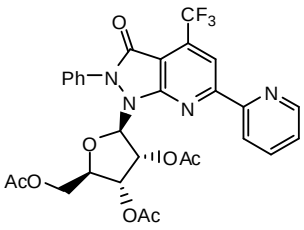
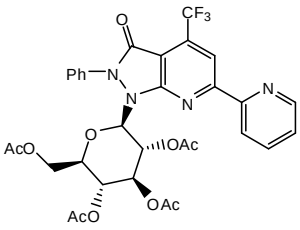
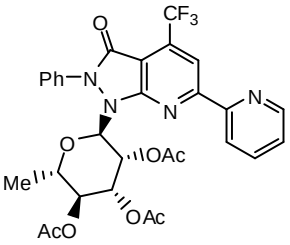
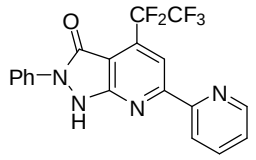
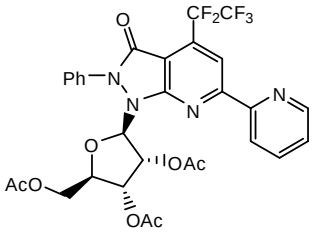
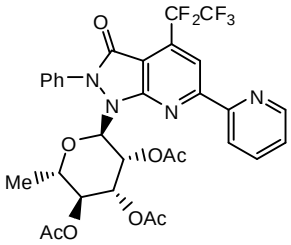
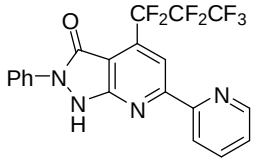
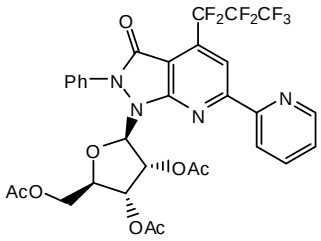
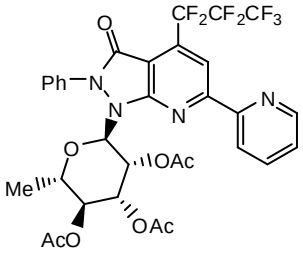
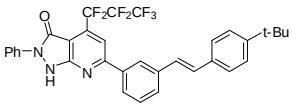
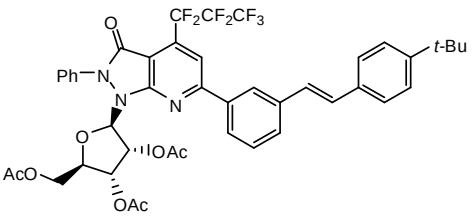
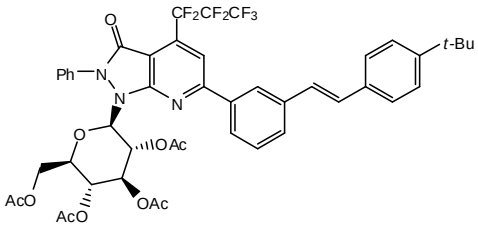
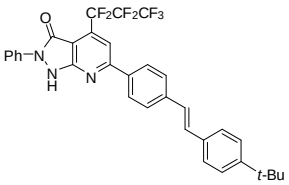
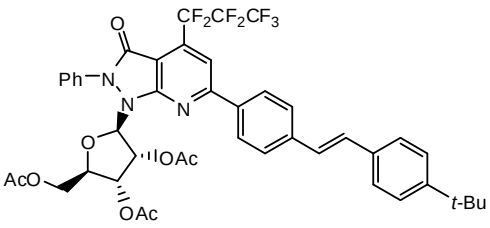
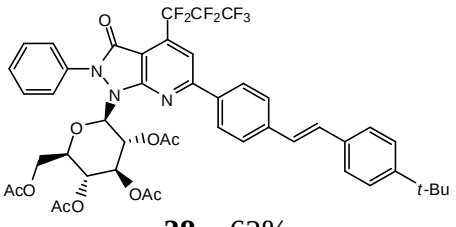
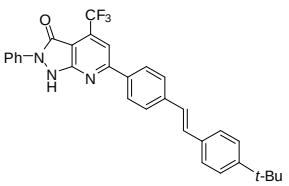
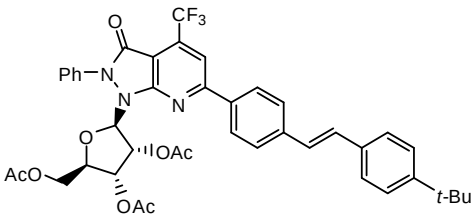
Scheme 19. Synthesis of nucleosides. Conditions: i – dry CH_3CN, BSA, TMSOTf, 82 ^oC, 2h.

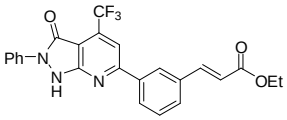
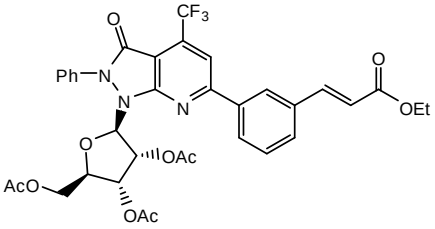
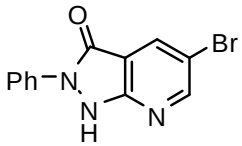
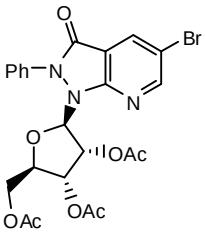
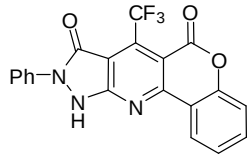
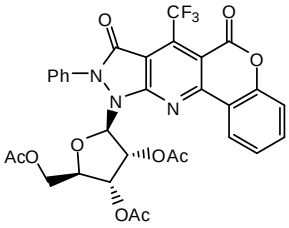
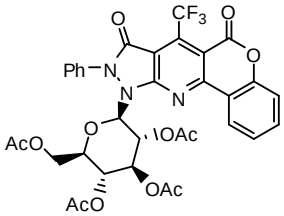
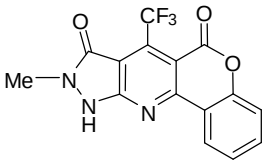
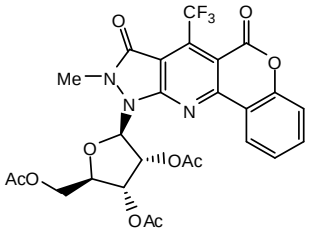
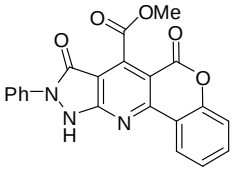
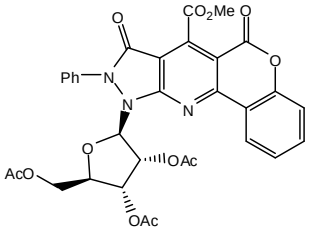
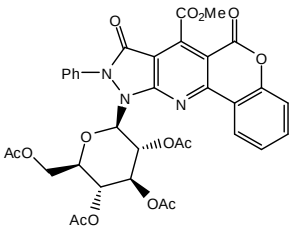
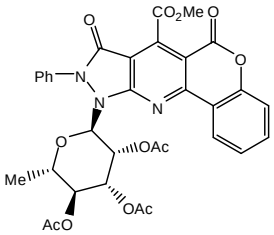
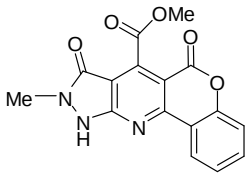
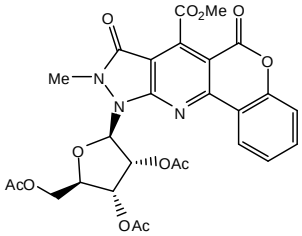
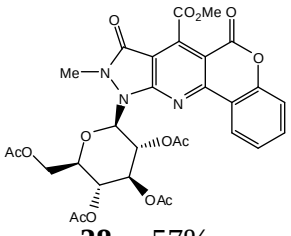
Likewise, other 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2, 9, 11,** and **33**, and dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones **22** were engaged in glycosylation reactions giving corresponding nucleosides **37-39**. An overwiev of successfuly isolated nucleosides is summarized in **Table 5**.

Table 5. Synthesis and yields of nucleosides **37-39**

	Product and yield [a]		
 **2a**	 **37a**, 80%	 **38a**, 76%	 **39a**, 68%
 **2c**	 **37b**, 80%	 **38b**, 80%	 **39b**, 44%
 **2d**	 **37c**, 69%	 **38c**, 78%	 **39c**, 58%
 **2f**	 **37d**, 92%		
 **2g**	 **37e**, 94%	 **38e**, 86%	 **39e**, 86%

	Product and yield [a]
 **2i**	 **37f**, 83%
 **2r**	 **37g**, 84%  **38g**, 74%  **39g**, 61%
 **2s**	 **37h**, 59%  **38h**, 69%  **39h**, 64%
 **2u**	 **37i**, 87%  **38i**, 94%  **39**i, 59%
 **2v**	 **37j**, 82%  **39j**, 85%
 **2w**	 **37k**, 76%

	Product and yield [a]		
 **2x**	 **37l**, 82%	 **38l**, 68%	 **39l**, 84%
 **2y**	 **37m**, 82%		 **39m**, 83%
 **2z**	 **37n**, 85%		 **39n**, 84%
 **9a**	 **37o**, 70%		 **38o**, 71%
 **9b**	 **37p**, 55%		 **38p**, 62%
 **9c**	 **37q**, 82%		

	Product and yield [a]
 **11a**	 **37r**, 79%
 **33a**	 **37s,** 64%
 **22a**	 **37t**, 76%  **38t**, 65%
 **22b**	 **37u**, 68%
 **22c**	 **37v**, 79%  **38v**, 73%  **39v**, 67%
 **22d**	 **37w**, 81%  **38w**, 57%

[a] – yields refer to pure isolated products

Reactions with ribose **34** and rhamnose **36** give better results than reactions with glucose **35**. Higher yields were observed for ribosides and rhamnosides and parallel decomposition seemed to be slower than in case of the synthesis of glucosides **38**. Also, **38** decomposes during storage.

All synthesized nucleosides were characterized by ^{1}H, ^{13}C NMR, IR spectral data as well as MS, HRMS and elemental analysis. Br-containing nucleoside **37s** was charachterised only by ^{1}H NMR since the compound proved to be unstable.

In case of **37f** and **37g**, structure was independantely confirmed by X-ray analysis. To simplify the view of structure, hydrogen atoms are not shown (**Figure 9**).

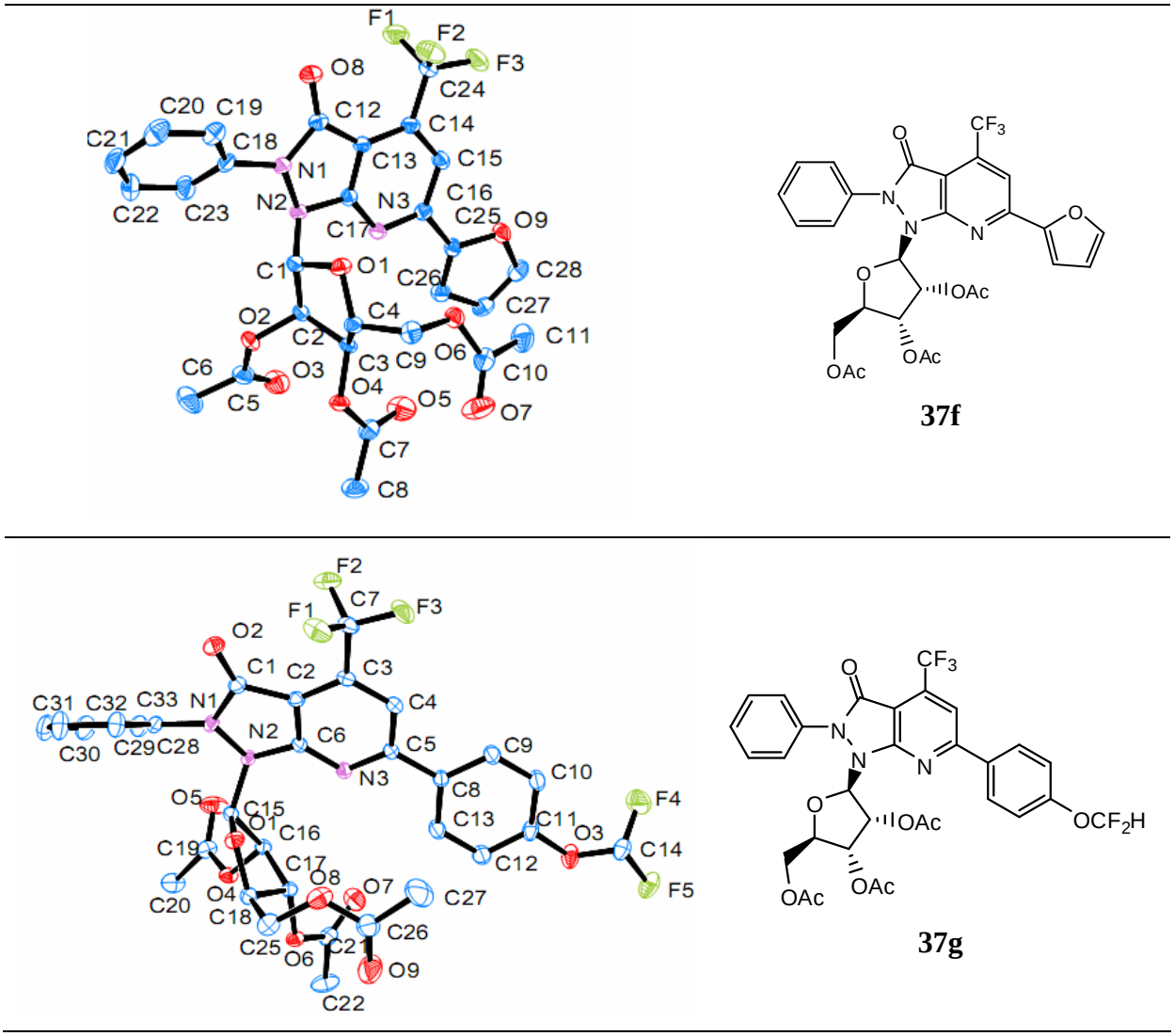
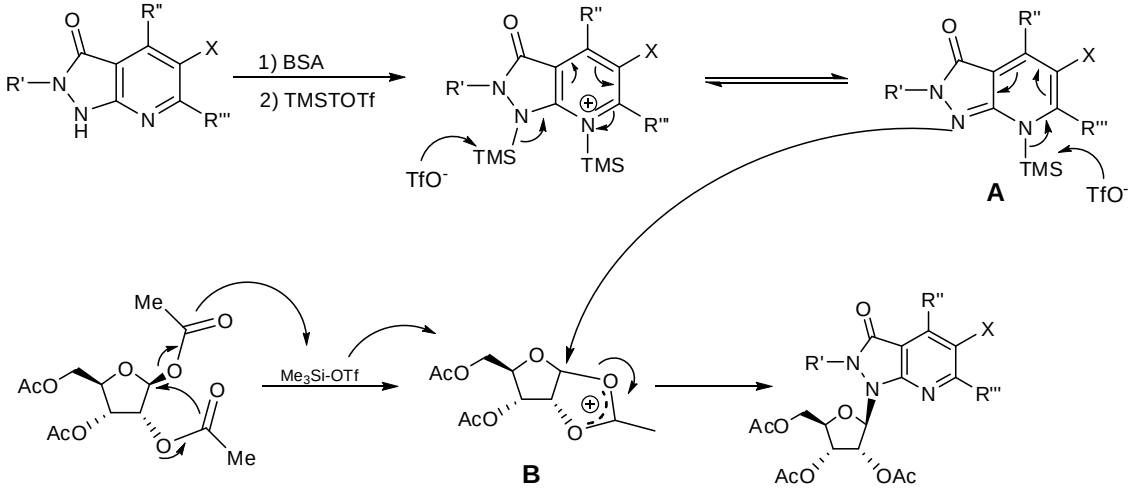


Figure 9. Ortep plot of **37f** and **37g**.

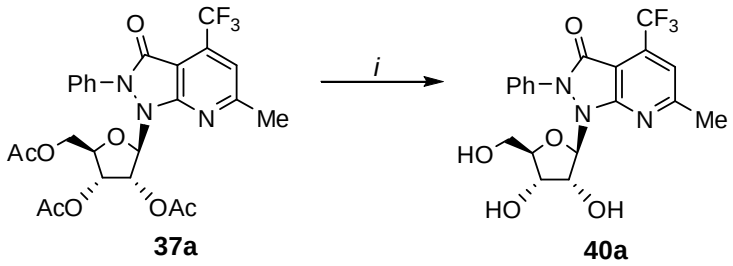
The possible mechanism of the reaction, and in agreement with that reported by Ostrovskyi,[87] is generally similar to the known mechanistic pathway for naturally occurring purines.[134] First, pyrazolo[3,4-*b*]pyridine-3-one is being silylated by BSA, subsequent rearrangement (intermediate **A**) by action of TMSOTf follows. Subsequently, intermediate **A** attacks cyclic cation **B**, which is formed *via* nucleophilic attack of the neighboring acetyl group on the deacetylated anomeric position of sugar. This results in formation of the desired nucleoside.



Scheme 20. Mechanism of glycosilation reaction.

The next task was the deprotection of the products. Several methods have been described, marking two as most effective:[135] cleavage of the acetyl group can be performed by hot aqueous methylamine [136] or ammonia in methanol.[137]

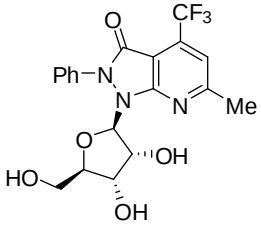
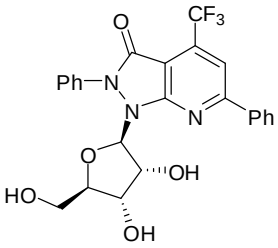
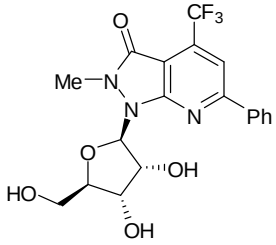
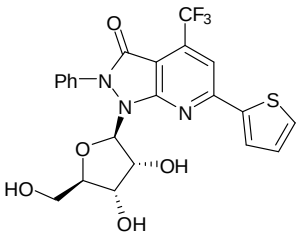
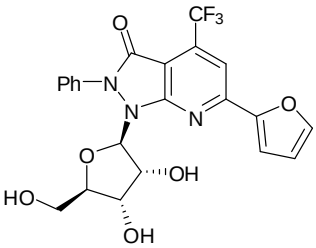
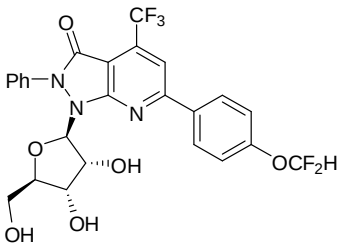
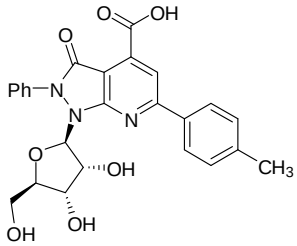
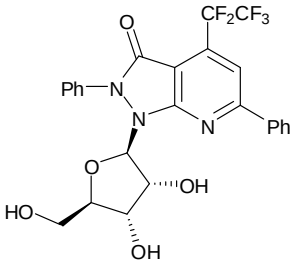
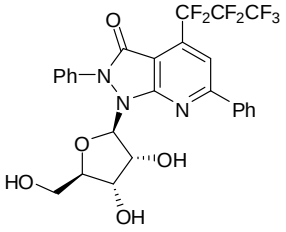
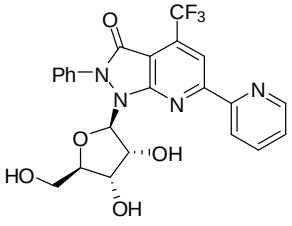
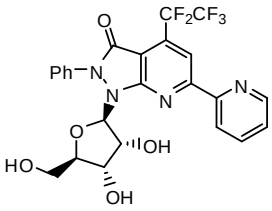
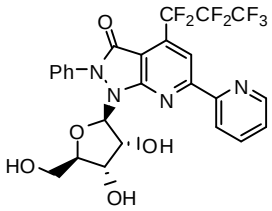
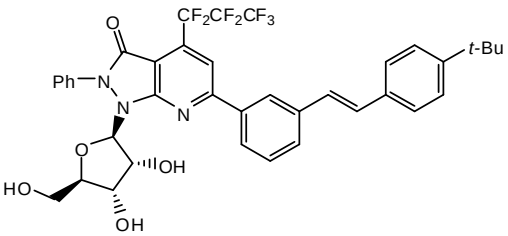
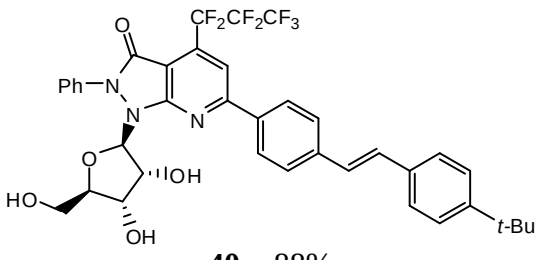
The second procedure required more continuous stirring (up to 24 hours), but it is milder thus lowering the possibility of decomposition of substrate. The only byproduct formed is acetamide, which can be easily separated by column chromatography or even by sublimation under vacuum. Therefore, we employed ammonia in methanol for deprotection of **37a** and an overnight stirring yielded in deprotected nucleoside **40a** (**Scheme 21**).



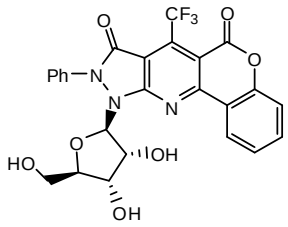
Scheme 21. Deprotection of acetylated nucleoside **37a**. *i* – NH_3/MeOH, RT, overnight.

The same procedure was successfully applied to afford other deprotected nucleosides **40-42**. Most of previously synthesized nucleosides were deacetylated in excellent yields (**Table 6**).

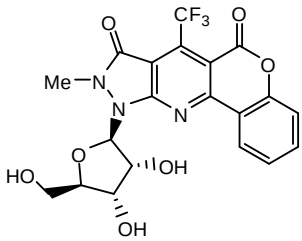
Table 6. Deprotected glycosides and yields

Product and yield [a]
Ribosides:
 **40a,** 96%
 **40b,** 92%
 **40c,** 95%
 **40e**, 89%
 **40f**, 93%
 **40g**, 98%
 **40i**, 89%
 **40j**, 91%
 **40k**, 85%
 **40l,** 93%
 **40m**, 91%
 **40n**, 92%
 **40o**, 92%
 **40p**, 88%

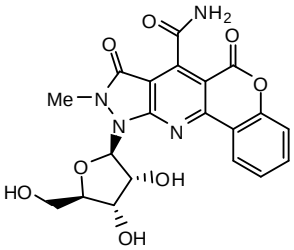
Product and yield [a]



40t, 95%

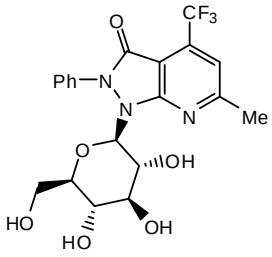


40u, 92%

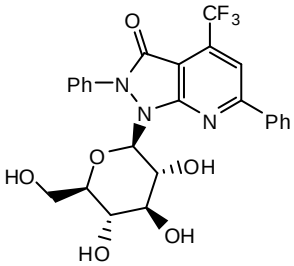


40w, 95%

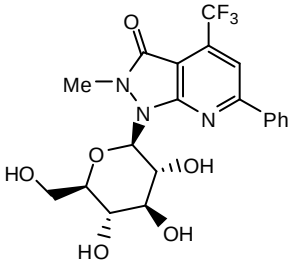
Glycosides:



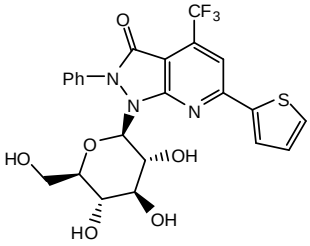
41a, 91%



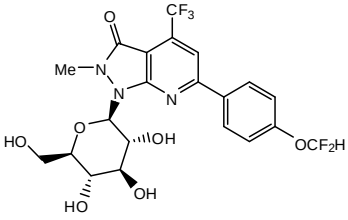
41b, 94%



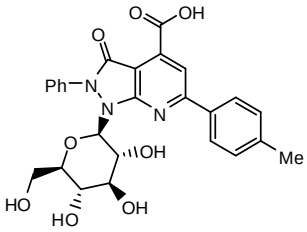
41c, 93%



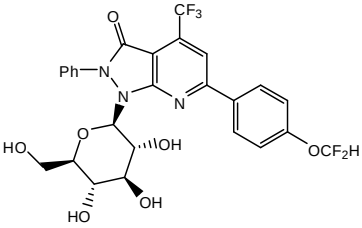
41e, 90%



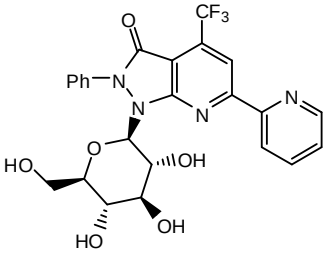
41h, 94%



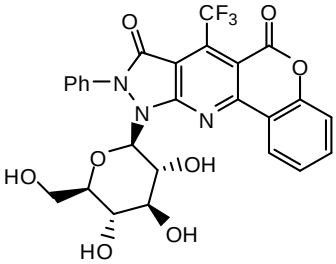
41i, 97%



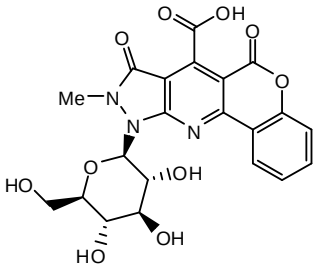
41g, 96%



41l, 85%

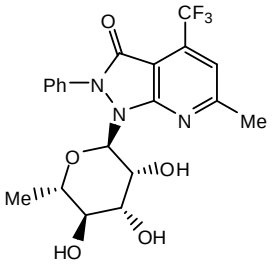


41t, 89%

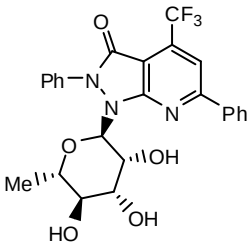


41w, 91%

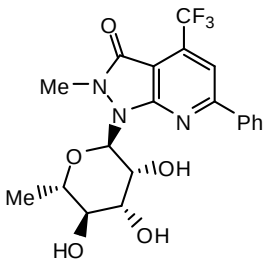
Product and yield [a]
Rhamnosides:



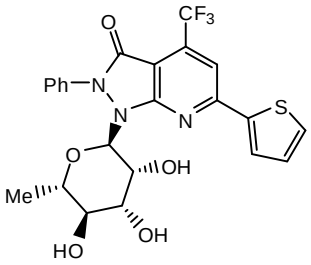
42a, 90%



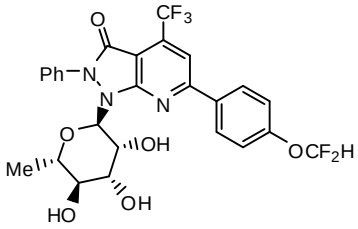
42b, 93%



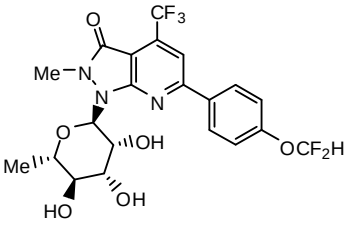
42c, 90%



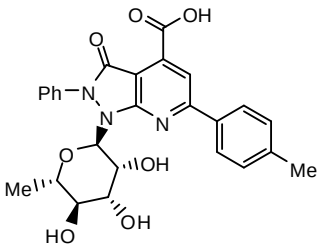
42e, 97%



42g, 88%



42h, 91%

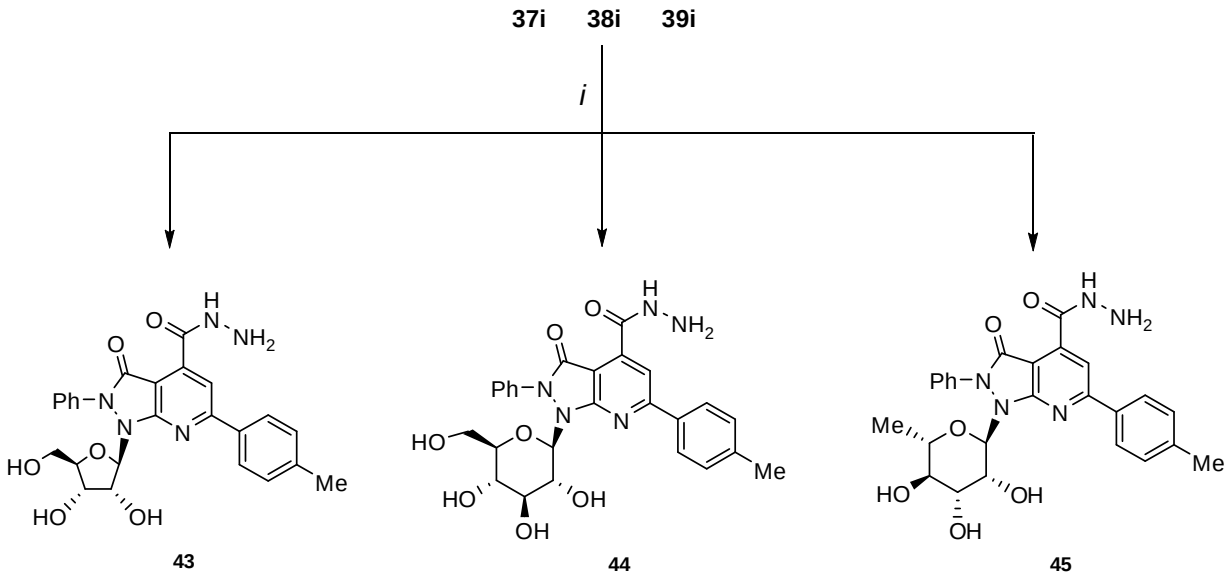


42i, 90%

[a] – yields refer to pure isolated products

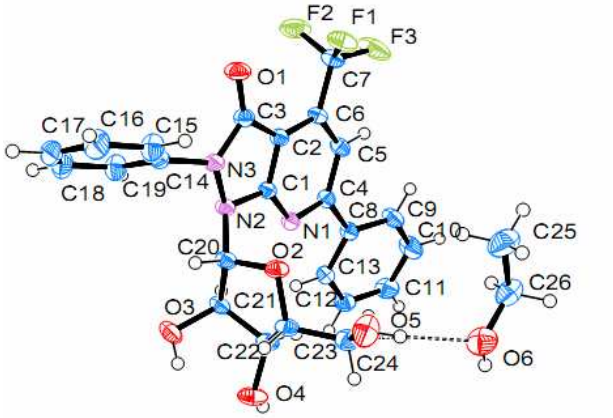
In case of 1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-2-methyl-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **37d** attempts of deprotection led to decomposition of substrate. The most possible explanation would be instability of pyridine ring because of prescence of two electron-withdrawing groups CF_3. Also deprotection of **37s,** a 5-bromo-substituted nucleoside, failed, since the compound decomposes during storage.

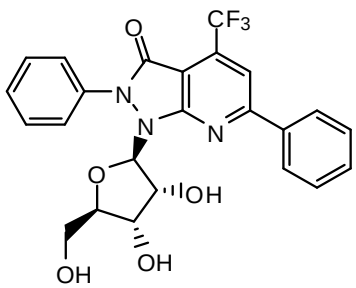
It is interesting that the ester group of glycosylated 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **4, 38i** and **39i** were transformed into primary amides. Introduction of the amide residue could only increase the binding affinity to the target enzyme. The ester group-containing molecules **37i**, **38i** and **39i** were also deprotected using hydrazine hydrate; besides cleavage of acetyl groups, transformation of ester group into corresponding hydrazide occured (**Scheme 22**). Products **43-45** were formed as yellow precipitates which could be easily filtrated and washed to afford the target product in quantitative yields.



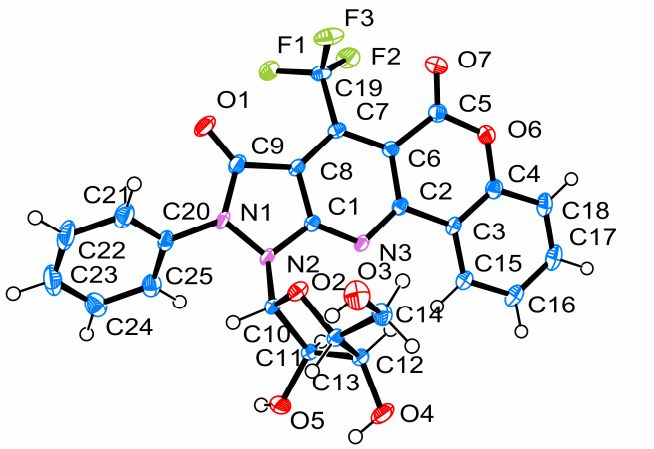
Scheme 22. Deprotection of acetylated nucleosides **37-39i**. *i* – N_2H_4•H_2O, MeOH, RT, 24h.

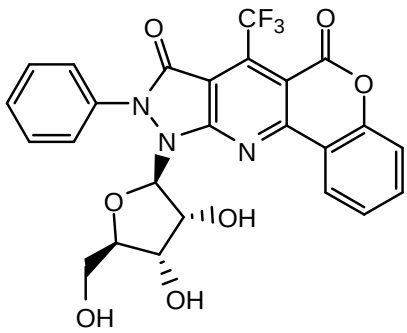
All deprotected nucleosides were charachterized using ^{1}H NMR, ^{13}C NMR, ^{19}F NMR techniques, also IR, mass and HRMS spectra were obtained as well as elemental analysis. 2D NMR measurements were performed to tie up C-H and O-H protons of sugar part with the signals of ^{1}H NMR. The structures of **40b, 40t** and **42g** were confirmed by X-ray analysis.



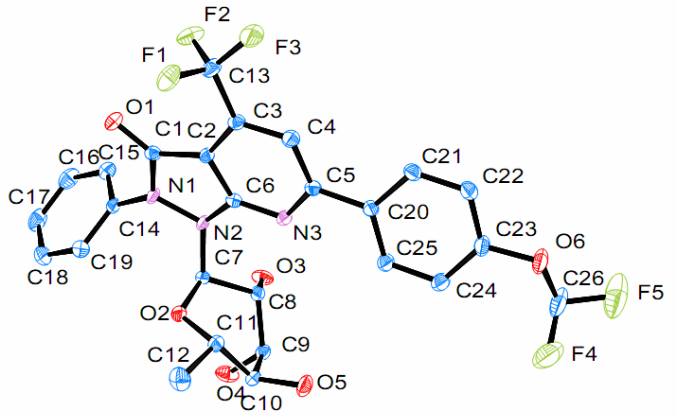


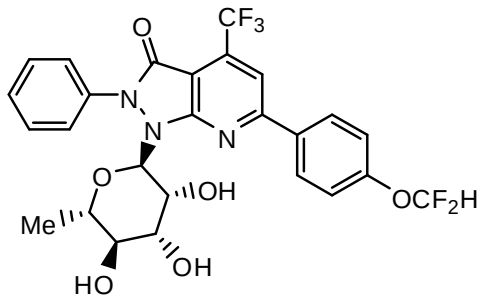
40b





40t





42g

Figure 10. Ortep plots of **40b** (solvate with EtOH)**, 40t** and **42g**.

In addition, the X-ray structure of **40t** represents a helpful proof of the structure of starting material **22a**, since 2D NMR measurements of **22a-d** could not be obtained because of low solubility, as indicated before.

2.2.2.2. Acyclic nucleosides

The interest in acyclic nucleosides began in the mid-1970s when Aciclovir was first reported as a potent anti-herpes drug.[138] Most of the antiviral compounds that are currently used in the treatment of HSV (herpes simplex virus), VZV (varicella zoster virus) and CMV (cytomegalovirus) can be described as acyclic nucleoside analogues. Among these agents, acyclovir and gancyclovir (**Figure 11**) were reported to be efficient antiviral agents with low host toxicity.[139] Also pencyclovir, a carba analogue of gancyclovir, were found to be more potent and highly selective antiviral agent against HSV and VZV.[140] These cyclovirs and their

analogues have stimulated extensive research in the synthesis of new acyclic analogues mimicking the sugar portion of naturally occurring nucleosides.[24]

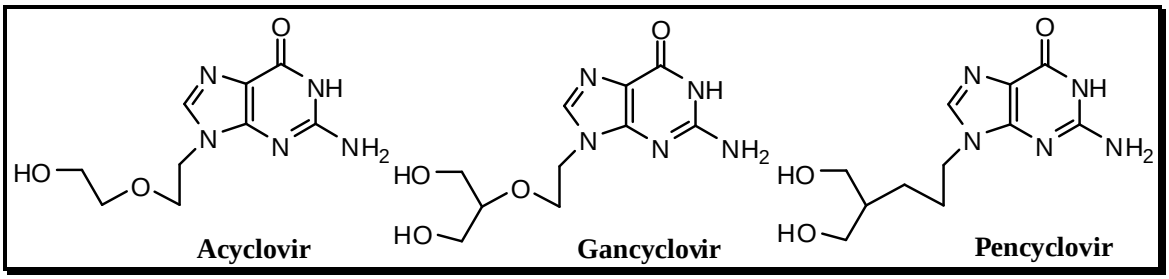


Figure 11. Acyclic nucleosides with antiviral activity.

ADA is an enzyme that catalyzes the hydrolytic deamination of various purine nucleosides but its use can be extended to carbocyclonucleosides or acyclonucleosides as well.[8a] A classic example of ADA inhibitor is *erythro*-9-(2-hydroxy-3-nonyl)adenine **46** which can be classified as acyclic nucleoside analogue.[5a] In another study, compounds **47** with a number of functionalized groups attached to the alkyl side chain, were evaluated as phosphate mimics on the basis of their ability to inhibit purine nucleoside phosphorylase (PNP).[141]

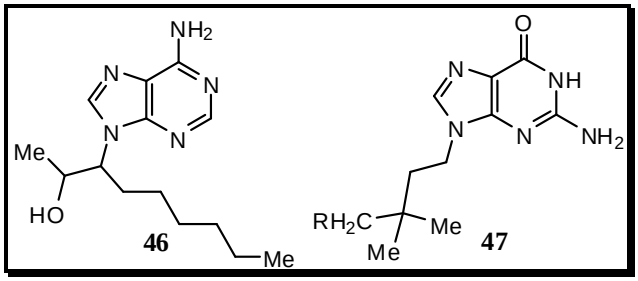
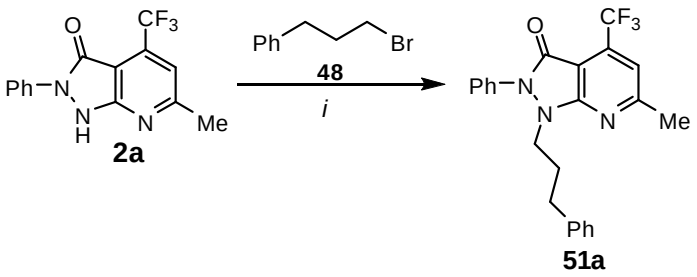


Figure 12. Biologically active acyclic analogues of nucleosides.

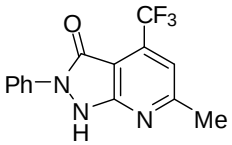
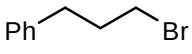
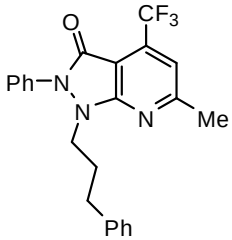
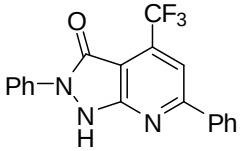
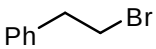
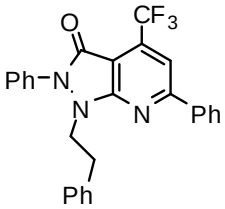
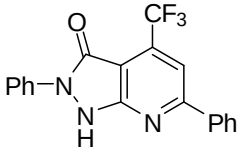
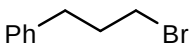
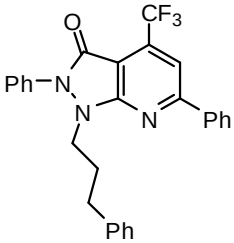
In present study alkyl chains were attached to position C1 of pyrazolo[3,4-*b*]pyridin-3-ones **2** by performing direct N-alkylation using different alkyl halides. Trial experiments showed that corresponding alkyl chlorides are too inactive to enter the reaction. Therefore, only bromides **48-50** were chosen for *N*-alkylation. Reaction between **2a** and (3-bromopropyl)benzene **48** resulted in according 1-alkyl-pyrazolo[3,4-*b*]pyridin-3-one **51a** (**Scheme 23**).

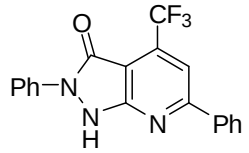
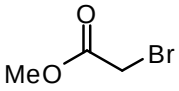
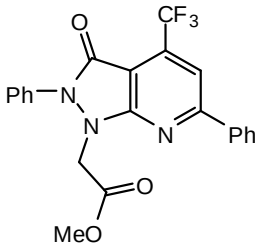
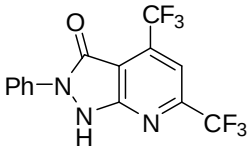
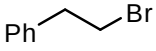
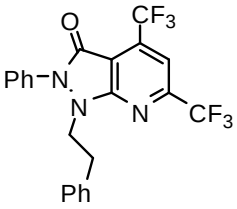
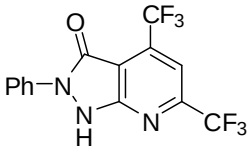
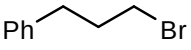
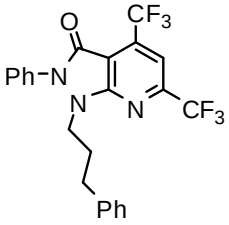


Scheme 23. Synthesis of 1-alkyl-pyrazolo[3,4-*b*]pyridin-3-one **51a**. *i* - K_2CO_3 (3eq), DMF, 90^oC, 6h.

Likewise, other 1-alkyl-pyrazolo[3,4-*b*]pyridin-3-ones **51b-f** were obtained in excellent yields (**Table 7**).

Table 7. Synthesis of 1-alkyl-pyrazolo[3,4-*b*]pyridin-3-ones **51 a-f**

		Yield (51)[a]
 **2a**	 **48**	 **51a**, 90%
 **2c**	 **49**	 **51b**, 89%
 **2c**	 **48**	 **51c**, 88%

		Yield (51)[a]
 **2c**	 **50**	 **51d**, 79%
 **2e**	 **49**	 **51e**, 87%
 **2e**	 **48**	 **51f**, 91%

[a] - yields refer to pure isolated products

1-Alkyl-pyrazolo[3,4-*b*]pyridin-3-ones **51** are bright yellow crystalline compounds with low melting points, except **51a** and **51f**, which are oils. Unlike starting materials **2**, compounds **51a–f** are soluble in many common organic solvents. The structures of all afforded compounds **51** were characterized by ^{1}H, ^{13}C, ^{19}F NMR, IR spectral data as well as MS, HRMS and elemental analysis. The structure of **51b** was independently confirmed by X-ray analysis (**Figure 13**).

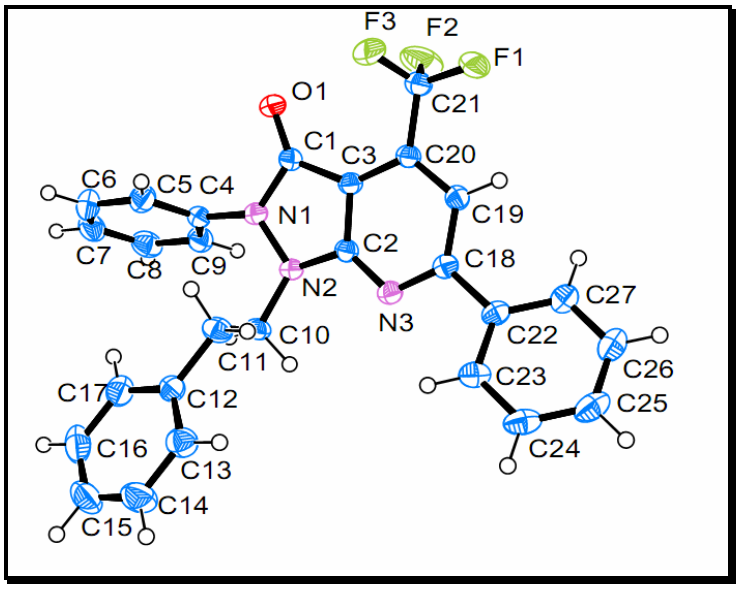
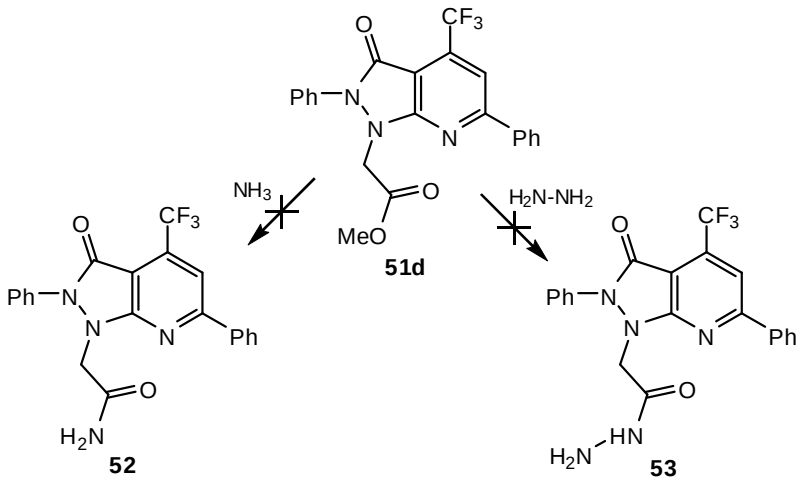


Figure 13. Ortep plot of 1-phenethyl-2,6-diphenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **51b**.

As mentioned before, the NH_2 group has an undisputable biological importance. Many drugs are designed to mimic or to interfere with the action of natural amine neurotransmitters. Therefore we decided to exchange the metoxy group of **51d** to an amino or hydrazine group. Compound **51d** was treated with saturated ammonia in methanol and hydrazine hydrate (**Scheme 24**). As the result, an undecipherable mixture of compounds was isolated; mass spectroscopy indicates some evidence towards polymerization, considering that the prescence of fragments with high mass was observed.



Scheme 24. Unsuccessful reactions of **51d**.

2.2.3. Conclusions

In a conclusion of this chapter, a number of new potential ADA and IMPDH inhibitors, nucleosides based on pyrazolo[3,4-*b*]pyridin-3-one core, were synthesized. Cyclic nucleosides were synthesized using a modified silyl Hilbert-Jones method while acyclic analogues were obtained using simple N-alkylation with alkyl bromides. Both cyclic and acyclic nucleosides, bearing an electron-withdrawing group at position C-4 and/or C-6 of aglycone moiety, possess potential biological activity. A number of tests, aiming biological evaluation of prepared substrates are currently in progress.

2.3. Synthesis of 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones

The subject of the present part of this work is the synthesis of 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones via catalytic hydrogenation of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones and corresponding nucleosides. Catalytic hydrogenation of dichromeno[4,3-*b*]pyrazolo[4,3-*e*]pyridine-6,8-diones and corresponding nucleosides is examined.

2.3.1. Introduction

One of the most popular strategies in drug design to reach the best inhibition of an enzyme is to mimic the transition state of its activity.[31e] Such purine analogues as conformycin **54**, pentostatin **55** and their analogues **56** and **57** (**Figure 14**) represent ADA transition-state analogous inhibitors [5c, 142, 143] un which show a strong, nearly irreversible interaction with the receptor.

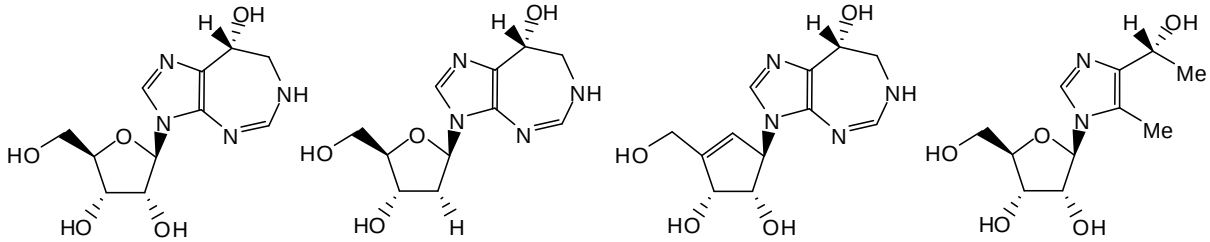


Figure 14. Purine analogues mimicking transition state of ADA activity.

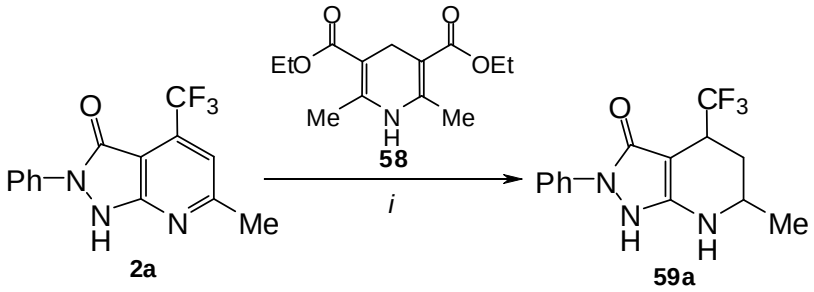
The studies suggest that purines and their isosters, which possess a tetrahedral carbon atom and bear a polar group coordinated to the Zn^{2+} ion (Zn^{2+} is known as cofactor of ADA), can be considered as potential ADA inhibitors. Several methods can be considered to afford a purine analogue bearing tetrahedrally coordinated carbon, but one of most convenient is preliminary construction of aromatic ring system and subsequent hydrogenation of target ring.

In 1955 Mauzerall and Westheimer[144] showed for the first time that 1,4-dihydropyridines, also known as Hantzsch esters,[145] are able to reduce carbonyl compounds by a direct hydrogen transfer to the substrate. Since then a broad range of transfer hydrogenations conducted with

Hantzsch esters in combination with different Lewis acids and additives has been reported.[146] Hydrogenation of substrates such as N-unprotected imines, enamines, and N-heteroaromatic compounds remained challenging until it was discovered that Brønsted acids may be used as activators of C=N bonds. Group of Rueping has made a great contribution in development of Brønsted acid catalyzed hydrogenations using Hantzsch esters as hydride source.[147]
Hantzsch esters are commonly known as synthetic analogues of nicotinamide adenine dinucleotide (NADH). NADH is an important co-factor in nature, which serves as a hydride source for a broad variety of reductions, including reductive aminations.[148]

2.3.2. Hydrogenation of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones

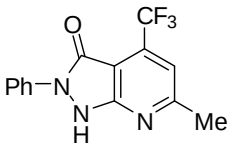
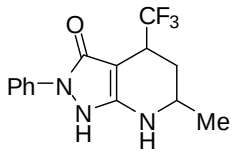
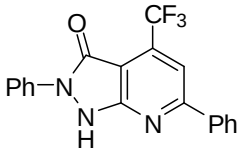
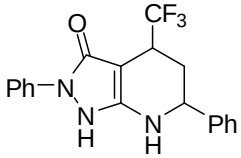
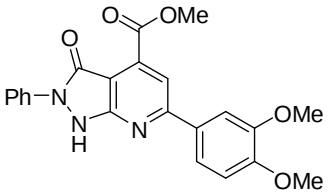
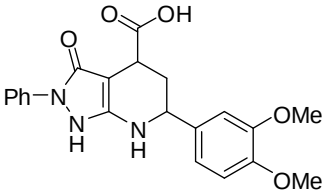
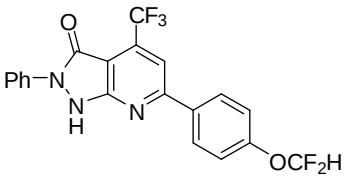
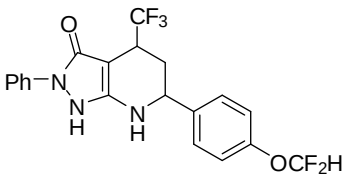
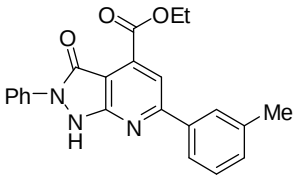
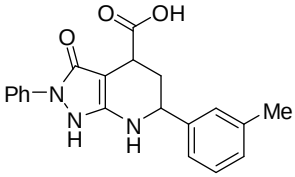
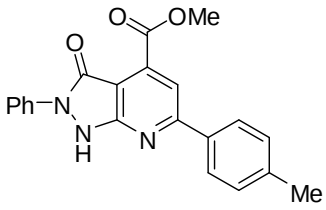
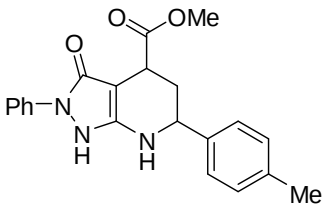
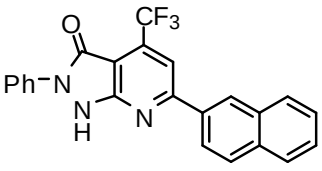
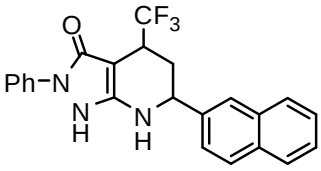
We studied the reduction of the pyridine ring of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2** following a described procedure[147c-e] using *p*-toluenesulphonic acid PTSA as catalyst (**Scheme 25**). Regardless of carcinogenic properties, benzene was chosen as solvent because it gave the highest yields of the reaction. Hantszch ester **58** was synthesized according to a classical but effective method developed in the 19th century[145].



Scheme 25. Hydrogenation of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **2a**. *i* – PTSA, benzene, 60 °C, 12h.

A number of previously synthesized 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2** were used for the hydrogenation reaction giving the desired products **59a-g** (**Table 8**).

Table 8. Synthesis of 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **59 a-g**

	Yield (59)[a]
 **2a**	 **59a**, 96%
 **2c**	 **59b**, 70%
 **2m**	 **59c**, 47%
 **2o**	 **59d**, 65%
 **2s**	 **59e**, 51%
 **2u**	 **59f**, 73%
 **2aj***	 **59g**, 57%

[a] yields refer to pure isolated products

*starting material provided by Zorik Chilingaryan

According to TLC, the reactions yielded single diastereomers. In addition, the NMR spectra do not indicate a mixture of diastereomers in the isolated products. The yields of products **59** are influenced by the presence of moisture and most probably by steric factors of substitute at C-6. All 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **59** were characterized by ^{1}H, ^{13}C NMR, and IR spectral data as well as by MS, HRMS and elemental analysis. 2D NMR measurements were performed, but no correlations were found which could unambigiously assign the isolated diastereomer. ^{19}F NMR spectroscopy also proved to be a convenient tool to control the conversion of the starting material during the reaction, since the chemical shift of the CF_3 group located at the sp^2 carbon is about -61 ppm while at its location at a sp^3 carbon results of a shift to -68 ppm. The structure of **59a** was confirmed by x-ray analysis (**Figure 15**).

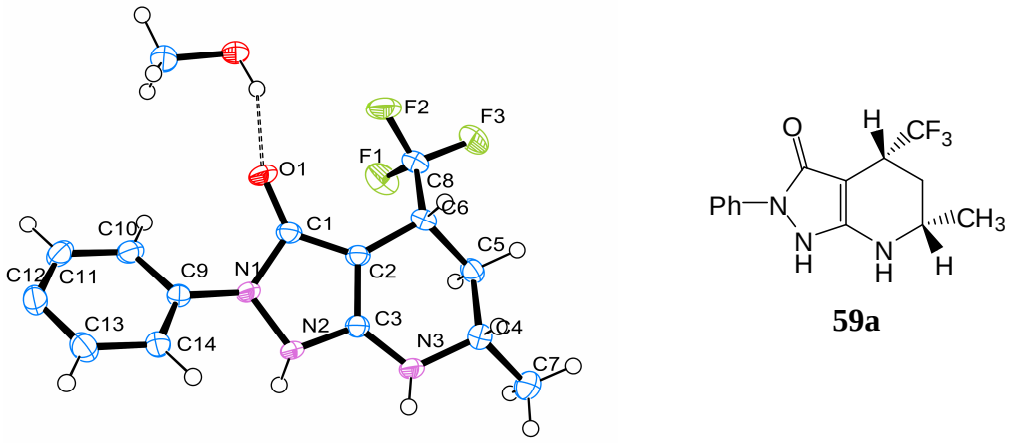
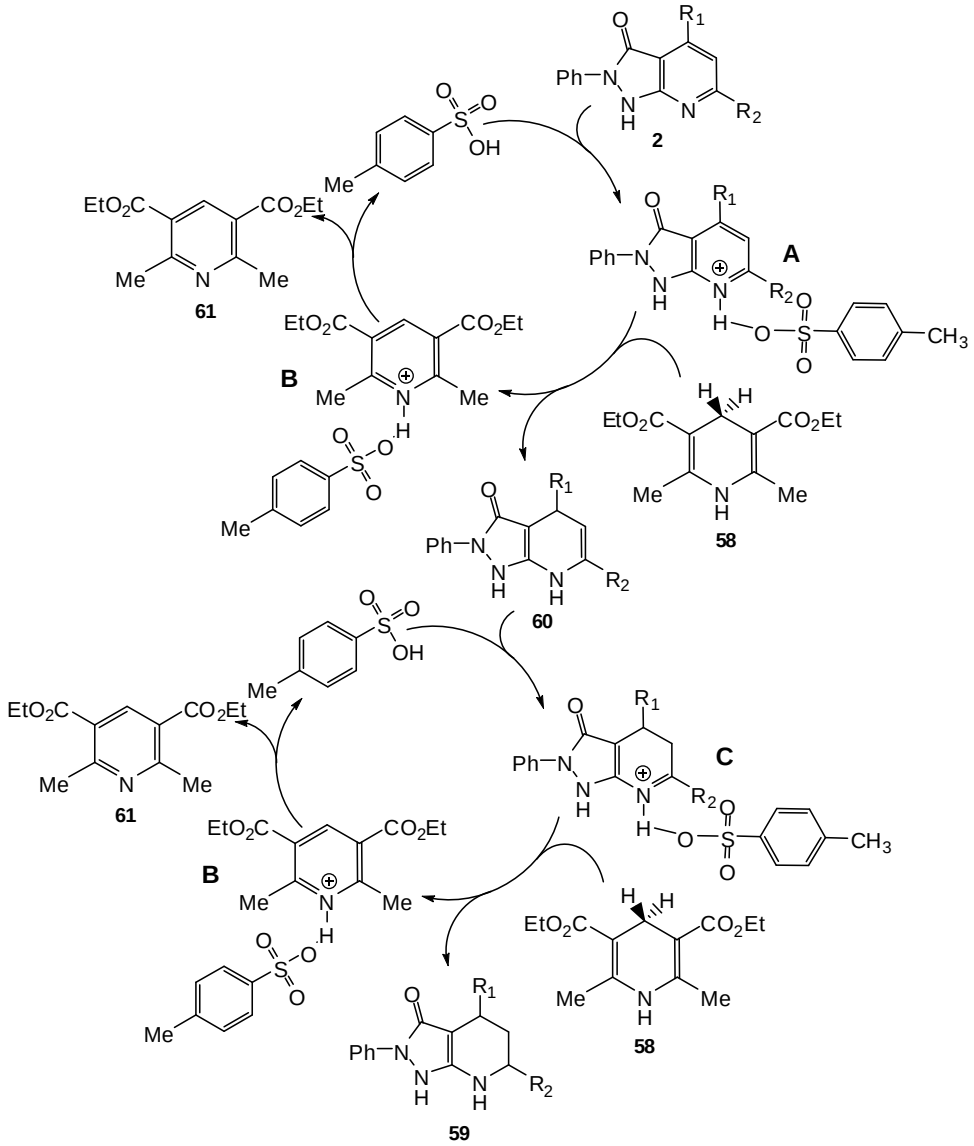


Figure 15. Ortep plot of **59a**. Crystal solvate with MeOH.

X-ray analysis shows that **59a** is solvated by methanol forming a hydrogen bond with the carbonyl moiety. It proves that the carbonyl group at position 2 of the pyrazolo[3,4-*b*]pyridin-3-one participates in hydrogen bonding probably will interact with the asparagine rest in the ADA's active pocket. The X-ray experiment shows that the product possesses a *trans* configuration.

The possible mechanism of the cascade hydrogenation is in agreement with the one proposed by Rueping[147d] as outlined in **Scheme 26**. The first step is protonation of the pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **2** through the PTSA to generate the iminium ion **A**. Subsequent transfer of the first hydride from the dihydropyridine **58** generates enamine **60** and pyridinium salt **B**, which undergoes proton transfer to regenerate PTSA and Hantzsch pyridine **61**. The enamine **60** reacts in a second cycle with PTSA to produce iminium **C**, which is again subjected to

hydride transfer to give the desired 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **59**. Subsequent proton transfer recycles PTSA and generates a second equivalent of the Hantzsch pyridine **61**. The formation of intermediates **A** and **C** in this mechanistic pathway explains the lower yields of hydrogenated products **59** in case of bulky substituents located at position 6. Because of steric reasons PTSA cannot stabilize the iminium cation.



Scheme 26. Mechanism of hydrogenation of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones **2**.

Unsuccessful experiments

Besides the above mentioned successful hydrogenations, a number of experiments failed. The substrates which proved to be inactive in the catalytic hydrogenation are listed below (**Figure 16**).

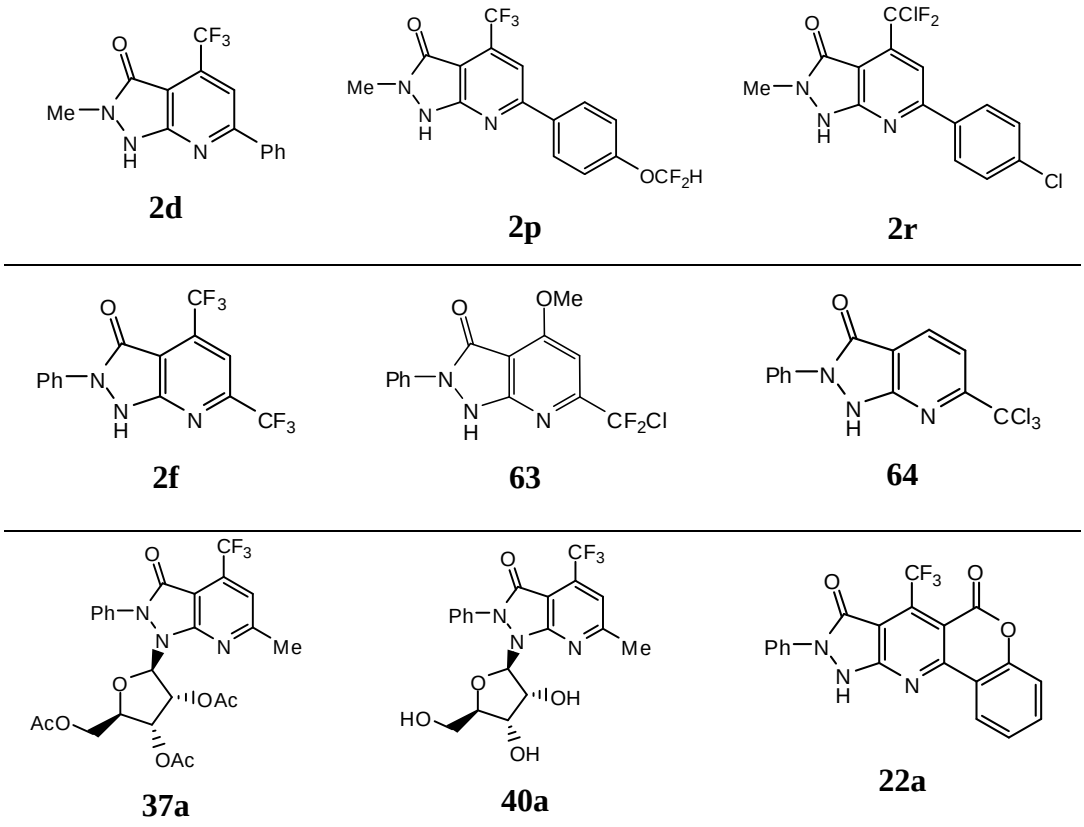


Figure 16. Compounds unable undergo cascade hydrogenation using Brønsted acid.

Unreactive compounds can be devided in three groups: first, compounds with bulky substituents near the pyridine nitrogen; second, substrates bearing electron-withdrawing groups at position C-6; third, insoluble substrates.

As indicated before, bulky substituents were probably the reason of low yields of **59**. Substituents as tetraacetylribose in **37a,** or deprotected ribose in **40a** or even the heavy structure of **22a** itself eliminates the possibility that catalyst could stabilize the iminium cation which leads to subsequent hydride attachment to a molecule.

Compounds **2f, 63** and **64** proved to be useless for hydrogenation. Electron-withdrawing substituent at C-6 prevents formation of the imminium cation since nitrogen has become less electron-rich.

The insolubility of some selected substrates led to failure of reaction. Unfortunately, after several try-outs we could not find a suitable solvent which could dissolve the substrate and provide a favourable environment for hydrogenation.

2.3.3. Conclusions

In a conclusion of the present chapter, the possibility and limitations of hydrogenation of pyridine ring of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones were studied. It was found that in order to perform successful hydrogenation of pyridine ring, nitrogen atom has to be spatially free, and neighbouring carbon has to be furnished with electron-donating group which favours formation of imminium cation and stabilizes it. Library of possible ADA and IMPDH inhibitors was supplemented with seven new 4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones, which represent transition-state of substrate, interfered either by ADA or IMPDH. Biological evaluation of these compounds is currently in progress.
Results outlined in the current chapter are a promising start for further experiments namely asymmetric hydrogenation using chiral Brønsted acids in order to obtain single diastereomers.

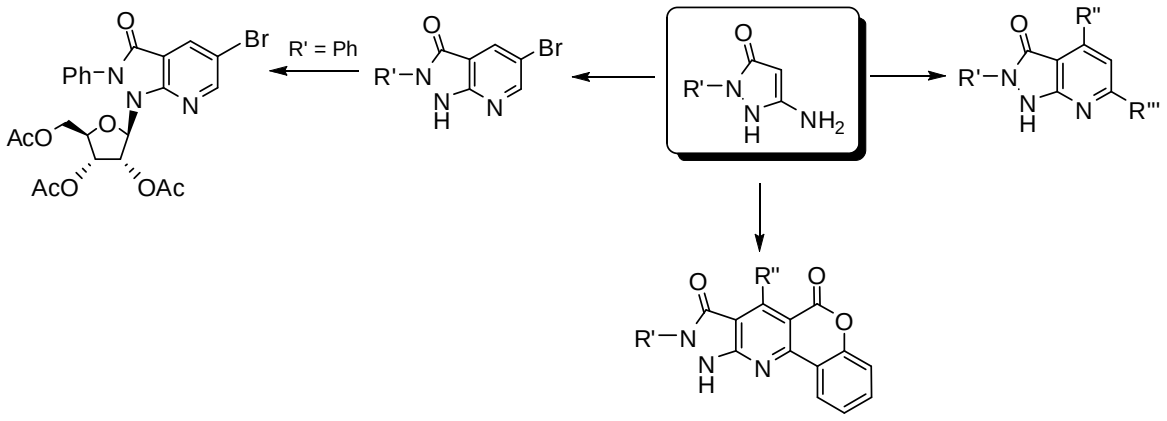
3. General conclusions and graphical overview

In a conclusion of this work, a variety of new deazapurine analogues and their nucleosides were synthesized. Bearing a strong electron withdrawing group, these compounds are potential inhibitors of ADA and IMPDH and may show a broad variety of biological activities.

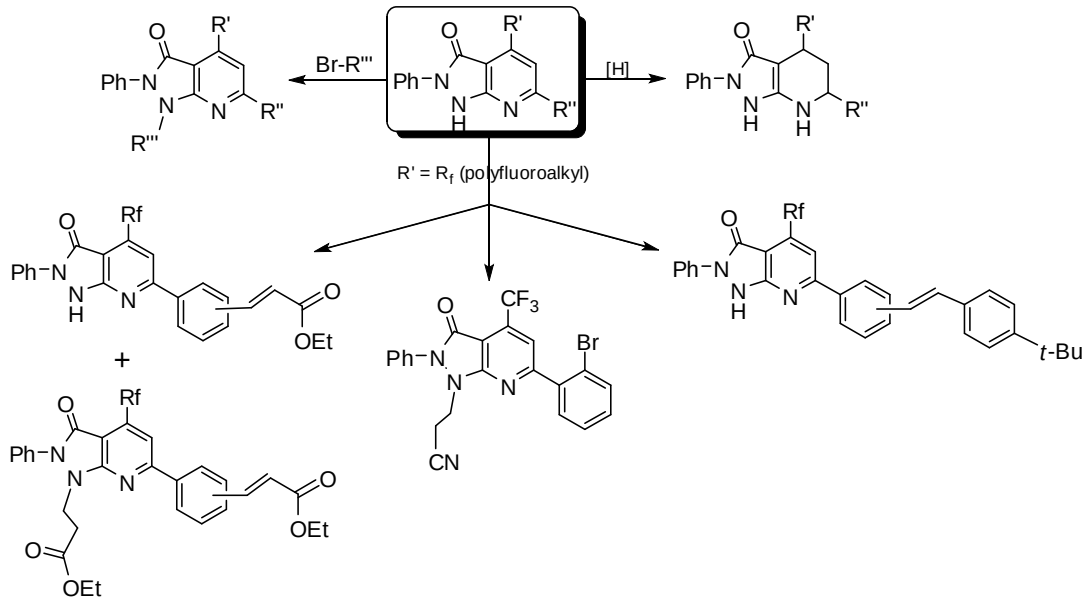
Most target substances are obtained in moderate to excellent yields via a classical approach involving [3+3] cyclocondesation of heterocycles containing an enamine fragment, such as aminopyrazolones. As bielectrophiles 1,3-diketones or 3-acyl-4-chlorocoumarines were used. Inverse electron demand Diels-Alder reactions were applied for the synthesis of 5-substituted pyrazolo[3,4-*b*]pyridin-3-ones. Modification of bromine-containing pyrazolo[3,4-*b*]pyridin-3-ones was performed using Pd-catalyzed reactions. Classical nucleosides were synthesized using a modified silyl Hilbert-Jones method, while acyclic analogues were obtained using *N*-alkylation with alkyl bromides. Cascade hydrogenation of 1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-ones using PTSA as catalyst and Hantzsch ester as hydride source was performed.

Preliminary biological evaluation in collaboration with Dr. Meyer zu Schwabedissen (University of Basel) indicates a potent activity of several newly synthesized compounds. Several representatives show strong antagonistic action on human smooth muscle cells. Most potent compounds are now under study as novel, cell-selective drug-candidate for endovascular implants.

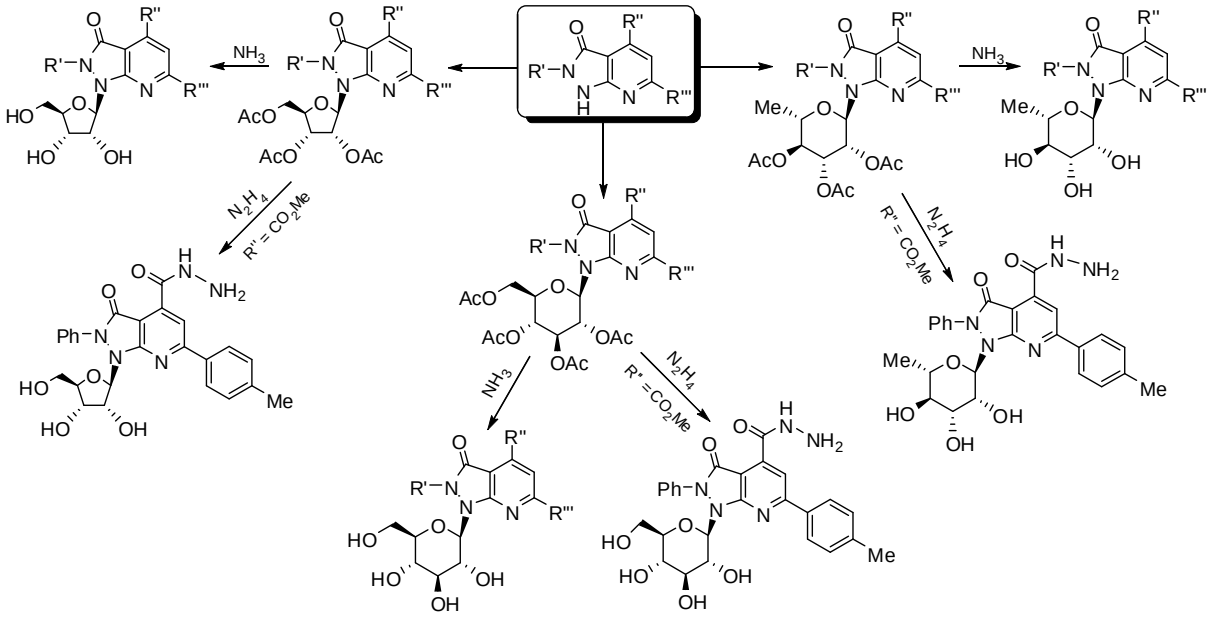
Schemes 27-30 give a brief overwiev of compounds synthesized in this work.



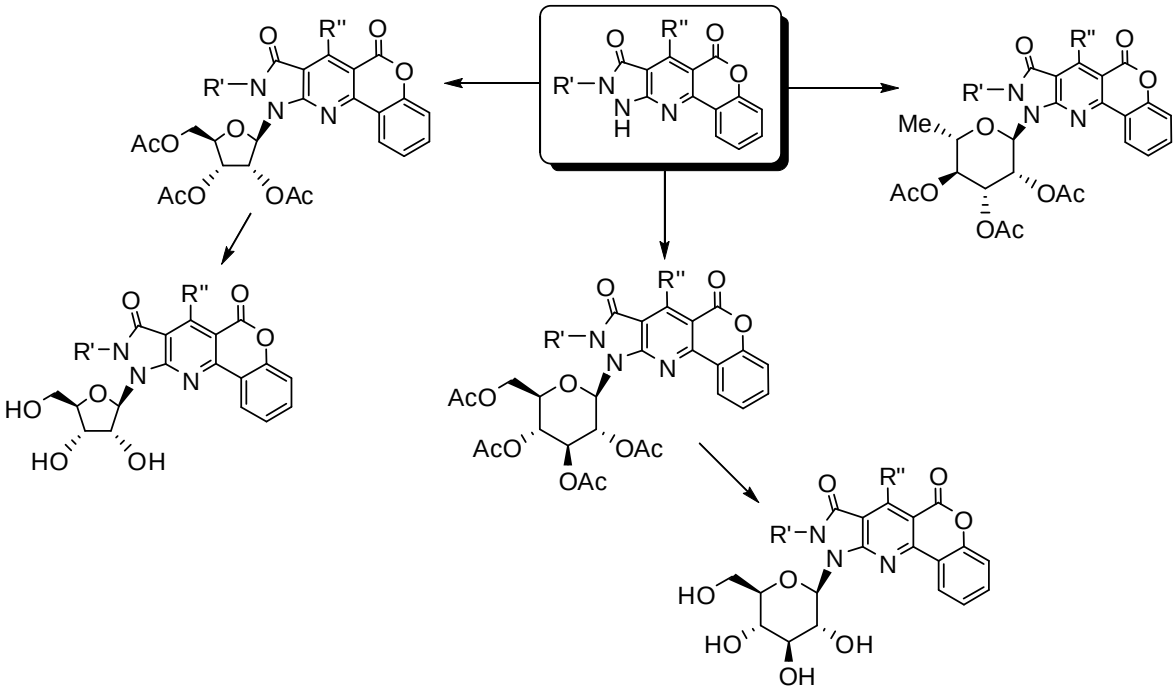
Scheme 27. 3-amino-1H-pyrazol-5(4H)-ones – useful building blocks for synthsesis of purine isosteres.



Scheme 28. Modification of pyrazolo[3,4-b]pyridin-3-ones.



Scheme 29. Synthesis of N-nucleosides of pyrazolo[3,4-b]pyridin-3-ones.



Scheme 30. Synthesis of N-nucleosides with potential biological importance.

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Appendix 1. Experimental Part

A.1. General: analytical equipment, chemicals and work technique

NMR Spectroscopy: ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on Bruker instruments AVANCE 250, ARX 300, and AVANCE 500 using the solvent internal standard ($CDCl_3$ 7.26 ppm and 77.16 ppm, DMSO-d_6 2.50 ppm and 39.52 ppm, $(CD_3)_2CO$ 2.05 ppm and 29.84 ppm). ^{19}F NMR spectra were recorded on AVANCE 250 and ARX 300 respectively considering $CFCl_3$ signal as a zero point of the scale. All chemical shifts are given in ppm. All coupling constants *J* are indicated in Hz. Multiplicities are given as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broad signal. More complex coupling patterns are represented by combinations of the respective symbols. For example, td indicates a triplet of doublets with the larger coupling constant associated with the first symbol (here: triplet).
The ^{1}H and ^{13}C NMR signals were assigned by DEPT and two-dimensional ^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY and ^{1}H-^{13}C correlation spectra (HMBC and HSQC).

Mass spectrometry (MS) and high resolution MS (HRMS):
a) Finnigan MAT 95 XP (Thermo Electron Corporation), EI, 70 eV;
b) GC 6890/ MS D 5973 (Agilent Technologies), MS(GC), 70 eV.

Infrared spectroscopy (IR): Nicolet 380 FT-IR spectrometer with ATR sampling technique for solids as well as liquids. Signal characterization: (w) = weak, (m) = medium, (s) = strong, (br) = broad.

Elemental analysis (EA): Flash EA 1112 (Thermoquest).

X-ray crystallography: Bruker Apex Kappa-II diffractometer with CCD camera (Mo-Kα radiation and graphite monochromator, λ = 0.71073 Å). The space group is determined by the XPREP program and the structures were solved via the SHELX-97 program package. Refinements were carried out according to the minimum square error method.

Thin layer chromatography (TLC): Merck HPTLC silica gel 60 F254 (aluminium sheets 20x20 cm). Detection with UV light at 254 and 366 nm; if necessary, development with

vanillin-sulfuric acid solution (1 g of vanillin, 14 mL of acetic acid and 1 mL of conc. sulfuric acid in 85 mL of methanol).

Melting Points: Micro heating table HMK 67/1825 Kuestner (Büchi apparatus). The melting points are uncorrected.

Column chromatography: Separation on Acros or Merck silica gel 60 Å (0.060-0.200 mm, 70-230 mesh). Eluents were distilled before use.

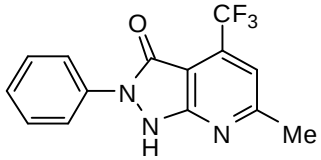
All chemicals and dry solvents were purchased from the standard chemical suppliers and used without further purification.

A.2. Procedures and spectroscopic data

A.2.1. General procedure for synthesis of compounds 2

Appropriate 5-amino-1*H*-pyrazol-3(2*H*)-one **4** (1 mmol) and corresponding 1,3-diketone **4** (1.2 mmol) were placed in a flask set with reflux and dissolved in AcOH (20 mL). The mixture was heated under reflux for 1-8 h (controlled by TLC). Then the solution was evaporated under reduced pressure, treated with H_2O, filtered, dried under reduced pressure and recrystallized from an appropriate solvent or subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

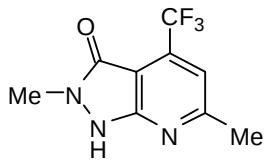
6-Methyl-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2a)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1,1,1-trifluoropentane-2,4-dione **6a** (185 mg, 1.2 mmol), **2a** was isolated via crystallization from isopropanol as gray crystals (249 mg, 82%); mp 181-182 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.64 (s, 3H, CH_3), 7.27 (t, $^3J_{H,H}$ = 7.8 Hz, 1H, Ph), 7.33 (s, 1H, H-5), 7.50 (t, $^3J_{H,H}$ = 7.8 Hz, 2H, Ph), 7.90 (d, $^3J_{H,H}$ = 7.8 Hz, 2H, Ph), 12.36 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 24.0 (CH_3), 102.6 (C-3a), 112.5 (C-5), 119.8 (CH_{Ar}), 121.8 (q, $^1J_{C,F}$ = 274.4 Hz, CF_3), 125.4, 129.0 (CH_{Ar}), 134.7 (q, $^2J_{C,F}$ = 35.3 Hz, $\underline{C}CF_3$), 137.1, 155.6 (C_{Ar}), 156.1 (C=O), 164.0 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.34 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3030 (w), 1644 (m), 1593 (w), 1499 (w), 1385 (w), 1278 (m), 1243 (m), 1148 (s), 1140 (s), 860 (m), 755 (m), 719 (m), 683 (s). MS (EI, 70 eV): *m/z* (%) = 295 (2) [M^++2], 294 (16) [M^++1], 293 (100) [M^+], 273 (15), 264 (52), 187 (7), 160 (6), 77 (28), 51 (8). HRMS (ESI): calcd for $C_{14}H_{11}F_3N_3O$ ([M+1]$^+$) 294.0849, found 294.0852. Anal. Calcd for $C_{14}H_{10}F_3N_3O$: C, 57.34; H, 3.44; N, 14.33. Found: C, 57.03; H, 3.39; N, 14.10.

2,6-Dimethyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2b)

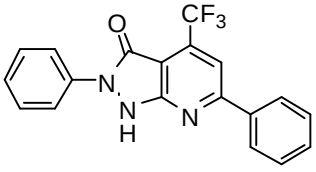


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 1,1,1-trifluoropentane-2,4-dione **6a** (185 mg, 1.2 mmol), **2b** was isolated via crystallization from isopropanol as gray solid (146 mg, 63%); mp 259-261 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.60 (s, 3H, CCH_3), 3.40 (s, 3H, NCH_3), 7.30 (s, 1H, H-5), 11.79 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 24.5 ($C\underline{C}H_3$), 30.3 (NCH_3), 101.1 (C-3a), 112.6 (C-5), 122.1 (q, $^1J_{C,F}$ = 274.0 Hz, CF_3), 128.6 (C-6), 133.5 (q, $^2J_{C,F}$ = 34.7

Hz, $\underline{C}CF_3$), 155.9 (C=O), 163.7 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.24 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2901 (w), 2683 (w), 1667 (w), 1628 (m), 1610 (s), 1435 (m), 1380 (m), 1328 (m), 1280 (m), 1244 (m), 1224 (m), 1146 (s), 1127 (s), 939 (m), 896 (w), 864 (m), 770 (m), 690 (m), 636 (m). MS (EI, 70 eV): *m/z* (%) = 232 (11) [M^++1], 231 (100) [M^+], 203 (29), 188 (6), 182 (6), 160 (23), 155 (7), 43 (7). HRMS (ESI): calcd for $C_9H_9F_3N_3O$ ([M+1]$^+$) 232.0692, found 232.0695. Anal. Calcd for $C_9H_8F_3N_3O$: C, 46.76; H, 3.49; N, 18.18. Found: C, 46.19; H, 3.14; N, 18.32.

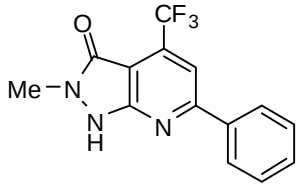
2,6-Diphenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2c)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,4-trifluoro-1-phenylbutane-1,3-dione **6b** (259 mg, 1.2 mmol), **2c** was isolated via crystallization from benzene as green crystals (348 mg, 98%); mp 172-173 °C.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.31 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ph), 7.51-7.57 (m, 5H, Ph), 7.89-7.92 (m, 2H, Ph), 8.01 (s, 1H, H-5), 8.25 (br s, 2H, Ph), 12.30 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 103.1 (C-3a), 110.7 (C-5), 120.0 (CH_{Ar}), 121.9 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 125.7, 127.6, 128.2, 129.0, 130.9 (CH_{Ar}), 135.1 (q, $^2J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 136.6, 136.6, 155.4 (C_{Ar}), 157.6 (C=O), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.17 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 1650 (m), 1593 (m), 1496 (m), 1371 (m), 1261 (s), 1190 (m), 1143 (s), 981 (m), 774 (m), 750 (s), 711 (m), 688 (s), 673 (s). MS (EI, 70 eV): *m/z* (%) = 357 (2) [M^++2], 356 (21) [M^++1], 355 (100) [M^+], 335 (13), 326 (35), 222 (6), 102 (6), 77 (21), 51 (5). HRMS (ESI): calcd for $C_{19}H_{13}F_3N_3O$ ([M+1]$^+$) 356.1005, found 356.1009. Anal. Calcd for $C_{19}H_{12}F_3N_3O$: C, 64.23; H, 3.40; N, 11.83. Found: C, 64.26; H, 3.38; N, 11.77.

2-Methyl-6-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2d)

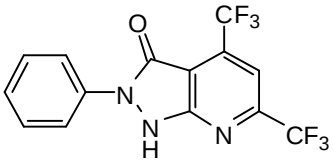


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 4,4,4-trifluoro-1-phenylbutane-1,3-dione **6b** (259 mg, 1.2 mmol), **2d** was isolated via crystallization from benzene as yellow crystals (217 mg, 74%); mp 318-320 °C.

^1H NMR (300 MHz, DMSO-d_6): δ = 3.45 (s, 3H, CH_3), 7.53-7.57 (m, 3H, Ph), 7.89 (s, 1H, H-5), 8.18-8.21 (m, 2H, Ph), 12.05 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 30.4 (CH_3), 102.0 (C-3a), 109.3 (q, $^3J_{C,F}$ = 5.5 Hz, C-5), 122.1 (q, $^1J_{C,F}$ = 275.1 Hz, CF_3), 127.5, 129.0, 130.7 (CH_{Ar}), 134.5 (q, $^2J_{C,F}$ = 35.3 Hz, $\underline{C}CF_3$), 137.0, 155.6 (C_{Ar}), 156.0 (C=O), 160.0 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.03 (s). IR (ATR,

cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2896 (w), 1666 (w), 1629 (m), 1607 (m), 1369 (m), 1276 (m), 1259 (m), 1236 (m), 1178 (m), 1133 (s), 856 (m), 766 (s), 686 (s). MS (EI, 70 eV): *m/z* (%) = 294 (16) [M^++1], 293 (100) [M^+], 265 (33), 222 (14), 102 (7), 77 (4), 51 (2). HRMS (EI): calcd for $C_{14}H_{10}F_3N_3O$ ([M]$^+$) 293.07705, found 293.077730. Anal. Calcd for $C_{14}H_{10}F_3N_3O$: C, 57.34; H, 3.44; N, 14.33. Found: C, 57.38; H, 3.49; N, 13.92.

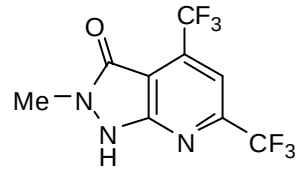
2-Phenyl-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2e)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1,1,1,5,5,5-hexafluoropentane-2,4-dione **6c** (250 mg, 1.2 mmol), **2e** was isolated via crystallization from benzene as yellow crystals (309 mg, 89%); mp 200-202 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.35 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ph), 7.53-7.58 (m, 2H, Ph), 7.84 (s, 1H, H-5), 7.87-7.90 (m, 2H, Ph), 12.77 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 107.6 (C-3a), 109.2 (C-5), 120.1 (CH_{Ar}), 120.7 (q, $^1J_{C,F}$ = 275.0 Hz, CF_3), 121.3 (q, $^1J_{C,F}$ = 275.4 Hz, CF_3), 126.4, 129.2 (CH_{Ar}), 135.9 (C_{Ar}), 138.3 (q, $^2J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 150.3 (q, $^2J_{C,F}$ = 35.3 Hz, $\underline{C}CF_3$), 154.1 (C=O), 155.7 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.13 (s, 3F, C=CCF_3), -66.62 (s, 3F, N=CCF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 3007 (w), 2917 (w), 1676 (w), 1661 (w), 1646 (w), 1604 (w), 1498 (w), 1273 (s), 1151 (s), 1140 (s), 992 (w), 890 (w), 752 (m), 684 (m). MS (EI, 70 eV): *m/z* (%) = 347 [M]$^+$ (100), 328 (13), 318 (33), 298 (12), 77 (20). HRMS (EI): calcd for $C_{14}H_7F_6N_3O$ ([M]$^+$) 347.05, found 347.0493. Anal. Calcd for $C_{14}H_7F_6N_3O$: C, 48.43; H, 2.03; N, 12.10. Found: C, 48.67; H, 1.96; N, 11.91.

2-Methyl-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2f)

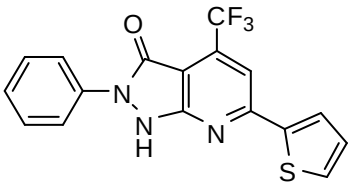


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 1,1,1,5,5,5-hexafluoropentane-2,4-dione **6c** (250 mg, 1.2 mmol), **2f** was isolated via crystallization from benzene as yellow crystals (245 mg, 86%); mp 236-238 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.51 (s, 3H, CH_3), 7.71 (s, 1H, H-5), 12.78 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 30.7 (CH_3), 106.2 (C-3a), 108.2 (C-5), 120.7 (q, $^1J_{C,F}$ = 274.9 Hz, CF_3), 121.3 (q, $^1J_{C,F}$ = 274.9 Hz, CF_3), 135.8 (q, $^2J_{C,F}$ = 36.5 Hz, $\underline{C}CF_3$), 149.2 (q, $^2J_{C,F}$ = 35.1 Hz, $\underline{C}CF_3$), 153.7 (C=O), 154.0 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.10 (s, C=CCF_3), -66.62 (s, N=CCF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2911 (w), 2655 (w), 1674 (w), 1639 (m), 1268 (m), 1232 (m), 1191 (m), 1144 (s), 1096 (m), 1005 (m), 941 (w), 879

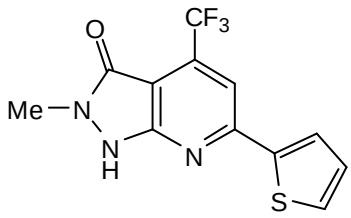
(m), 773 (m), 745 (w), 700 (m), 667 (m), 640 (m). MS (EI, 70 eV): *m/z* (%) = 286 (16) [M^++1], 285 (100) [M^+], 266 (28), 242 (13), 236 (28), 214 (16), 195 (12), 163 (15), 144 (14), 133 (14). HRMS (EI): calcd for $C_9H_5F_6N_3O$ ([M]$^+$) 285.03313, found 285.032980. Anal. Calcd for $C_9H_5F_6N_3O$: C, 37.91; H, 1.77; N, 14.76. Found: C, 37.71; H, 1.87; N, 14.58.

2-Phenyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2g)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,4-trifluoro-1-(thiophen-2-yl)butane-1,3-dione **6c** (267 mg, 1.2 mmol), **2g** was isolated via crystallization from benzene as yellow crystals (293 mg, 81%); mp 207-208 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.25-7.31 (m, 2H, Ar/Hetar), 7.48-7.54 (m, 2H, Ar/Hetar), 7.86-7.88 (m, 2H, Ar/Hetar), 7.89-7.90 (m, 1H, Ar/Hetar), 8.02 (1H, s, H-5), 8.25 (1H, dd, $^3J_{H,H}$ = 4.0 Hz, $^4J_{H,H}$ = 1.0 Hz, Hetar), 12.31 (1H, s, H-1). ^{13}C NMR (62.8 MHz, DMSO-d_6): δ = 102.4 (C-3a), 109.5 (t, $^3J_{C,F}$ = 5.0 Hz, C-5), 119.9 (CH_{Ar}), 121.8 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 125.6, 128.9, 129.1, 129.8, 131.9 (CH_{Ar}), 135.0 (q, $^2J_{C,F}$ = 35.8 Hz, $\underline{C}CF_3$), 136.6, 142.5, 155.4 (C_{Ar}), 156.6 (C=O), 157.4 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.27 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2863 (w), 1645 (m), 1588 (m), 1532 (w), 1497 (w), 1425 (m), 1398 (m), 1377 (m), 1348 (w), 1262 (m), 1234 (m), 1178 (m), 1140 (s), 1093 (m), 966 (w), 750 (m), 717 (s), 680 (m). MS (EI, 70 eV): *m/z* (%) = 362 (20) [M^++1], 361 (100) [M^+], 341 (11), 332 (26), 77 (18). HRMS (ESI): calcd for $C_{17}H_{11}F_3N_3OS$ ([M+1]$^+$) 362.05694, found 362.0574. Anal. Calcd for $C_{17}H_{10}F_3N_3OS$: C, 56.51; H, 2.79; N, 11.63. Found: C, 56.59; H, 2.74; N, 11.48.

2-Methyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2h)

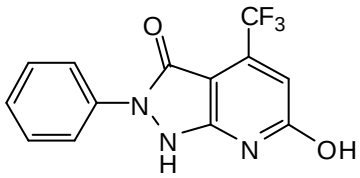


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 4,4,4-trifluoro-1-(thiophen-2-yl)butane-1,3-dione **6d** (267 mg, 1.2 mmol), **2h** was isolated via crystallization from benzene as yellow crystals (275 mg, 92%); mp 354-356 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): 3.41 (s, 3H, CH_3), 7.24 (dd, $^3J_{H,H}$ = 5.1 Hz, $^3J_{H,H}$ = 3.8 Hz, 1H, Hetar), 7.83 (dd, $^3J_{H,H}$ = 5.1 Hz, $^3J_{H,H}$ = 1.1 Hz, 1H, Hetar), 7.90 (s, 1H, H-5), 8.17 (dd, $^3J_{H,H}$ = 3.8 Hz, $^3J_{H,H}$ = 1.1 Hz, 1H, Hetar) 12.07 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 30.3 (CH_3), 101.6 (C-3a), 108.3 (q, $^3J_{C,F}$ = 5.3 Hz, C-5), 121.9 (q, $^1J_{C,F}$ = 274.5 Hz,

CF_3), 129.0, 129.2, 131.3 (CH_{Hetar}), 134.4 (q, $^2J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 142.7, 155.5 (C_{Ar}), 155.6 (C=O), 155.7 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.13 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2881 (w), 2673 (w), 1651 (w), 1627 (w), 1605 (m), 1538 (w), 1423 (m), 1378 (w), 1349 (w), 1289 (w), 1261 (m), 1239 (m), 1149 (m), 1130 (s), 1065 (w), 1035 (w), 941 (w), 849 (m), 710 (m), 690 (s). MS (EI, 70 eV): *m/z* (%) = 300 (15) [M^++1], 299 (87) [M^+], 298 (100), 271 (27), 256 (35), 228 (19), 227 (26), 108 (19). HRMS (ESI): calcd for $C_{12}H_9F_3N_3OS$ ([M+1]$^+$) 300.04129, found 300.04143. Anal. Calcd for $C_{12}H_8F_3N_3OS$: C, 48.16; H, 2.69; N, 14.04. Found: C, 48.20; H, 2.73; N, 13.83.

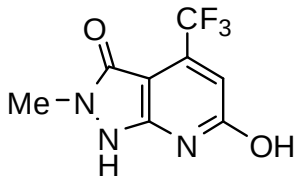
6-Hydroxy-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2i)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and ethyl 4,4,4-trifluoro-3-oxobutanoate **6e** (221 mg, 1.2 mmol), **2i** was isolated via crystallization from toluene as colorless solid (154 mg, 52%); mp 296-298 °C.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.53 (s, 1H, H-5), 7.22-7.28 (m, 1H, Ph), 7.45-7.51 (m, 2H, Ph), 7.71-7.74 (m, 2H, Ph), 11.77 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 102.3 (C-3a), 112.5 (C-5), 120.1 (CH_{Ar}), 121.6 (q, $^1J_{C,F}$ = 274.2 Hz, CF_3), 125.3, 129.0 (CH_{Ar}), 135.6 (C_{Ar}), 136.4 (q, $^2J_{C,F}$ = 33.4 Hz, $\underline{C}CF_3$), 137.2 (C_{Ar}), 155.3 (C=O), 164.8 (C-7a). ^{19}F NMR (235 MHz, DMSO-d_6): δ = -63.07 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (br w), 2991 (w), 2849 (w), 2713 (w), 1651 (m), 1594 (m), 1585 (m), 1537 (w), 1496 (w), 1463 (m), 1358 (m), 1283 (m), 1194 (m), 1160 (m), 1140 (s), 1082 (w), 988 (m), 908 (w), 956 (m), 780 (m), 750 (m). MS (EI, 70 eV): *m/z* (%) = 296 (19) [M^++1], 295 (100) [M^+], 275 (15), 266 (20), 132 (13), 77 (70), 51 (14), 29 (16). HRMS (ESI): calcd for $C_{13}H_9F_3N_3O_2$ ([M+1]$^+$) 296.06414, found 296.06449. Anal. Calcd for $C_{13}H_8F_3N_3O_2$: C, 52.89; H, 2.73; N, 14.23. Found: C, 53.00; H, 2.80; N, 14.11.

6-Hydroxy-2-methyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2j)

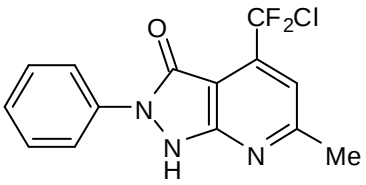


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and ethyl 4,4,4-trifluoro-3-oxobutanoate **6e** (221 mg, 1.2 mmol), **2j** was isolated via crystallization from benzene as colorless solid (180 mg, 77%); mp 299-301 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.41 (s, 3H, CH_3), 6.34 (s, 1H, H-5), 12.13 (s, 2H, NH, OH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.0 (CH_3), 108.2 (C-3a), 113.5 (C-5), 119.6 (C-6), 124.6 (q, $^1J_{C,F}$ = 274.0 Hz, CF_3), 134.7 (q, $^2J_{C,F}$ = 34.8 Hz, CCF_3), 150.7 (C=O), 163.5 (C-

7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -63.45 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2929 (br w), 2482 (br), 1651 (w), 1644 (m), 1584 (w), 1563 (m), 1434 (m), 1373 (w), 1336 (w), 1284 (s), 1254 (s), 1231 (s), 1207 (m), 1187 (s), 1140 (s), 1055 (w), 1025 (m), 949 (m), 905 (m), 862 (m), 713 (m), 605 (m). MS (EI, 70 eV): *m/z* (%) = 234 (7) [M^++1], 233 (100) [M^+], 232 (15), 213 (60), 190 (21), 171 (27), 143 (20), 142 (12), 92 (20), 64 (12), 43 (57). HRMS (ESI): calcd for $C_8H_7F_3N_3O_2$ ([M+1]$^+$) 234.04849, found 234.04891. Anal. Calcd for $C_8H_6F_3N_3O_2$: C, 41.21; H, 2.59; N, 24.45. Found: C, 41.58; H, 2.71; N, 24.19.

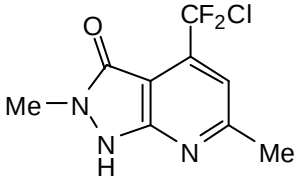
4-(Chlorodifluoromethyl)-6-methyl-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2k)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-chloro-1,1-difluoropentane-2,4-dione **6f** (205 mg, 1.2 mmol), **2k** was isolated via crystallization from toluene as gray solid (198 mg, 64%); mp 162-164 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.64 (s, 3H, CH_3), 7.24-7.29 (m, 2H, Ar), 7.48-7.53 (m, 2H, Ar), 7.89-7.92 (m, 2H, Ar), 12.30 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 24.4 (CH_3), 100.1 (C-3a), 110.8 (C-5), 123.3 (t, $^1J_{C,F}$ = 290.0 Hz, CF_2Cl), 127.5, 129.0, 130.7 (CH_{Ar}), 137.0 (C_{Ar}), 139.6 (t, $^2J_{C,F}$ = 29.0 Hz, $\underline{C}CF_2Cl$), 155.8 (C_{Ar}), 155.9 (C=O), 163.5 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -50.67 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3418 (w), 2667 (w), 1651 (m), 1589 (s), 1487 (m), 1359 (m), 1306 (s), 1278 (m), 1208 (s), 1112 (m), 1033 (m), 970 (s). MS (EI, 70 eV): *m/z* (%) = 311 (36) [M^++2], 310 (18) [M^++1], 309 (100) [M^+], 289 (21), 280 (18), 274 (13), 245 (15), 77 (39). HRMS (EI): calcd for $C_{14}H_{10}ClF_2N_3O$ ([M]$^+$) 309.04750, found 309.048136. Anal. Calcd for $C_{14}H_{10}ClF_2N_3O$: C, 54.29; H, 3.25; N, 13.57. Found: C, 54.46; H, 3.18; N, 13.37.

4-(Chlorodifluoromethyl)-2,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2l)

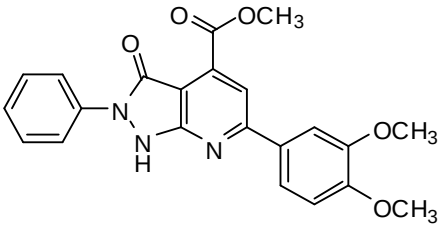


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 1-chloro-1,1-difluoropentane-2,4-dione **6f** (205 mg, 1.2 mmol), **2l** was isolated via crystallization from benzene as yellow solid (269 mg, 74%); mp 256-258 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.59 (s, 3H, CCH_3), 3.40 (s, 3H, NCH_3), 7.22 (s, 1H, H-5), 11.76 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 24.5 ($C\underline{C}H_3$), 30.3 (NCH_3), 100.1 (C-3a), 110.8 (C-5), 123.4 (t, $^1J_{C,F}$ = 290.9 Hz, CF_2Cl), 139.7 (t, $^2J_{C,F}$ = 29.5 Hz, $\underline{C}CF_2Cl$), 155.9 ($\underline{C}CH_3$), 156.0 (C=O), 163.6 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -50.27 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2911 (w), 2725 (w), 1661 (w), 1627 (m), 1605 (s), 1432 (w),

1410 (w), 1376 (m), 1327 (w), 1280 (w), 1208 (m), 1115 (s), 1035 (m), 964 (s), 833 (s), 753 (s). MS (EI, 70 eV): *m/z* (%) = 249 (34) [M^++2], 248 (14) [M^++1], 247 (100) [M^+], 219 (26), 212 (23), 176 (11), 160 (10), 43 (8). HRMS (ESI): calcd for $C_9H_9ClF_2N_3O$ ([M+1]$^+$) 248.0397, found 248.04. Anal. Calcd for $C_9H_8ClF_2N_3O$: C, 43.65; H, 3.26; N, 16.97. Found: C, 43.79; H, 3.16; N, 16.70.

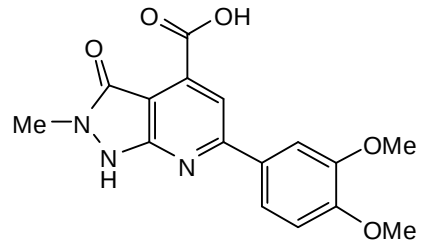
Methyl 6-(3,4-dimethoxyphenyl)-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine-4-carboxylate (2m)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and methyl 4-(3,4-dimethoxyphenyl)-2,4-dioxobutanoate **6g** (320 mg, 1.2 mmol), **2m** was isolated via crystallization from benzene as orange solid (284 mg, 70%); mp 165-167 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.85 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 7.11-7.14 (m, 1H, Ar), 7.27 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.48-7.54 (m, 2H, Ar), 7.79-7.85 (m, 2H, Ar), 7.89-7.94 (m, 3H, Ar), 11.86 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 52.8, 55.6 (OCH_3), 103.8 (C-3a), 110.3, 111.7, 112.2, 119.6, 120.8, 125.3, 129.0 (CH_{Ar}), 129.4, 137.1, 139.1, 149.0, 151.3 (C_{Ar}), 156.7 (C=O), 160.3 (C-7a), 165.5 ($\underline{C}O_2CH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 2841 (w), 1678 (w), 1586 (m), 1516 (m), 1446 (m), 1427 (m), 1281 (m), 1255 (s), 1219 (s), 1152 (m), 1040 (m), 1022 (m), 761 (s), 691 (m). MS (EI, 70 eV): *m/z* (%) = 406 (25) [M^++1], 405 (100) [M^+], 361 (15), 347 (19), 345 (31), 77 (16). HRMS (ESI): calcd for $C_{22}H_{20}N_3O_5$ ([M+1]$^+$) 406.1407, found 406.1408. Anal. Calcd for $C_{22}H_{19}N_3O_5$: C, 65.18; H, 4.72; N, 10.37. Found: C, 65.48; H, 4.74; N, 10.34.

6-(3,4-dimethoxyphenyl)-2-methyl-3-oxo-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid (2n)

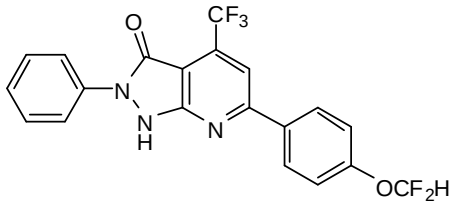


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and methyl 4-(3,4-dimethoxyphenyl)-2,4-dioxobutanoate **6g** (320 mg, 1.2 mmol), **2n** was isolated via crystallization from isopropanol as yellow solid (280 mg, 85%); mp 316-318 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.59 (s, 3H, NCH_3), 3.84 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 7.08 (d, $^3J_{H,H}$ = 8.5 Hz, 1H, Ar), 7.67-7.73 (m, 2H, Ar), 7.95 (s, 1H, H-5), 12.96 (s, 1H, NH), 16.22 (s, 1H, OH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 31.1 (NCH_3), 55.5, 55.6

(OCH_3), 102.2 (C-3a), 110.0, 111.7, 113.9, 120.7 (CH_{Ar}), 129.4, 137.0, 149.0, 151.2, 153.9 (C_{Ar}), 157.0 (C=O), 160.5 (C-7a), 164.3 (CO_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3078 (w), 2944 (w), 1717 (w), 1620 (m), 1589 (s), 1515 (m), 1428 (m), 1417 (m), 1354 (m), 1238 (s), 1217 (s), 1143 (m), 1024 (m), 766 (s). MS (EI, 70 eV): *m/z* (%) = 330 (20) [M^++1], 329 (93) [M^+], 286 (32), 285 (100), 284 (33), 270 (13), 242 (13), 227 (9). HRMS (ESI): calcd for $C_{16}H_{16}N_3O_5$ ([M+1]$^+$) 330.1084, found 330.1083. Anal. Calcd for $C_{16}H_{15}N_3O_5$: C, 58.36; H, 4.59; N, 12.76. Found: C, 58.65; H, 4.61; N, 12.70.

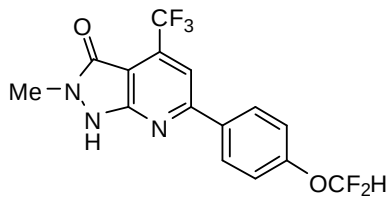
6-(4-(Difluoromethoxy)phenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2o)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(4-(difluoromethoxy) phenyl)-4,4,4-trifluorobutane-1,3-dione **6h** (339 mg, 1.2 mmol), **2o** was isolated via crystallization from benzene as yellow solid (291 mg, 69%); mp 179-181 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.29 (t, $^1J_{F,H}$ = 73.7 Hz, OCF_2H), 7.31-7.38 (m, 3H, Ar), 7.50-7.56 (m, 2H, Ar), 7.91-7.95 (m, 3H, H-5, Ar), 8.31 (d, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar), 12.03 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 102.8 (C-3a), 110.1 (q, $^3J_{C,F}$ = 5.6 Hz, C-5), 115.7 (t, $^1J_{C,F}$ = 258.9 Hz, OCF_2H), 118.6, 119.9, 125.3, 128.6, 129.2 (CH_{Ar}), 133.4 (C_{Ar}), 135.1 (q, $^2J_{C,F}$ = 35.0 Hz, $\underline{C}CF_3$), 136.5 (C_{Ar}), 152.7 (t, $^3J_{C,F}$ = 4.0 Hz, $\underline{C}OCF_2H$), 155.2 (C_{Ar}), 157.4 (C=O), 160.0 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.10 (s, 3F, CF_3), -82.72 (s, 2F, OCF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3070 (w), 1666 (m), 1598 (m), 1486 (w), 1373 (m), 1278 (m), 1262 (m), 1233 (m), 1184 (m), 1140 (s), 1122 (s), 1037 (s), 982 (m), 841 (m), 813 (m), 754 (s), 714 (s), 673 (s). MS (EI, 70 eV): *m/z* (%) = 422 (22) [M^++1], 421 (100) [M^+], 392 (23), 77 (53), 51 (21). HRMS (ESI): calcd for $C_{20}H_{13}F_5N_3O_2$ ([M+1]$^+$) 422.09224, found 422.09288. Anal. Calcd for $C_{20}H_{12}F_5N_3O_2$: C, 57.01; H, 2.87; N, 9.97. Found: C, 56.99; H, 3.05; N, 9.98.

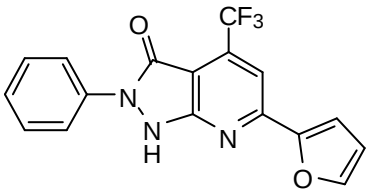
2-Methyl-6-(4-(difluoromethoxy)phenyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2p)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4b** (175 mg, 1 mmol) and 1-(4-(difluoromethoxy)phenyl)-4,4,4-trifluorobutane-1,3-dione **6h** (339 mg, 1.2 mmol), **2p** was isolated via crystallization from benzene as yellow solid (356 mg, 99%); mp >375 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.44 (s, 3H, CH_3), 7.31-7.36 (m, 2H, Ar), 7.38 (t, $^{1}J_{F,H}$ = 74.0 Hz, 1H, OCF_2H), 7.91 (s, 1H, H-5), 8.26-8.30 (m, 2H, Ar), 12.04 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 30.4 (CH_3), 102.2 (C-3a), 109.4 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.0 Hz, OCF_2H), 118.6 (CH_{Ar}), 122.0 (q, $^{1}J_{C,F}$ = 275.0 Hz, CF_3), 129.4 (CH_{Ar}), 133.6 (C_{Ar}), 134.6 (q, $^{2}J_{C,F}$ = 35.8 Hz, $\underline{C}CF_3$), 152.9 (t, $^{3}J_{C,F}$ = 3.0 Hz, $\underline{C}OCF_2H$), 155.6 (C_{Ar}), 155.9 (C=O), 159.1 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.01 (s, 3F, CF_3), -82.65 (s, 2F, CF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2929 (w), 2767 (w), 1668 (w), 1632 (m), 1584 (m), 1435 (m), 1371 (m), 1244 (m), 1227 (m), 1133 (s), 1049 (m), 839 (m), 770 (m), 702 (w), 648 (m), 623 (m) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 360 (17) [M^++1], 359 (100) [M^+], 331 (41), 288 (9), 51 (11), 43 (8). HRMS (EI): calcd for $C_{15}H_{10}F_5N_3O_2$ ([M]$^+$) 359.06877, found 359.06824. Anal. Calcd for $C_{15}H_{10}F_5N_3O_2$: C, 50.15; H, 2.81; N, 11.70. Found: C, 50.40; H, 2.65; N, 11.58.

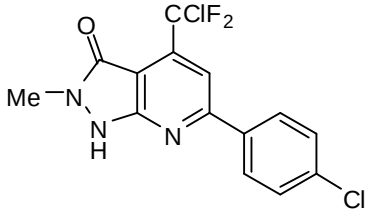
6-(Furan-2-yl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2q)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,4-trifluoro-1-(furan-2-yl)butane-1,3-dione **6i** (247 mg, 1.2 mmol), **2q** was isolated via crystallization from benzene as yellow crystals (307 mg, 89%); mp 192-193 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.78 (dd, 1H, $^{3}J_{H,H}$ = 3.5 Hz, $^{4}J_{H,H}$ = 1.7 Hz, Hetar), 7.30 (t, $^{3}J_{H,H}$ = 7,4 Hz, 1H, Ar), 7.50-7.55 (m, 3H, Ar/Hetar), 7.77 (s, 1H, H-5), 7.87-7.90 (m, 2H, Ar/Hetar), 8.04 (d, $^{4}J_{H,H}$ = 1.7 Hz, 1H, Hetar), 12.31 (s, 1H, H-1). ^{13}C NMR (62.8 MHz, DMSO-d_6): δ = 102.4 (C-3a), 108.8 (C-5), 113.2, 113.6, 119.9 (CH_{Ar}), 121.7 (q, $^{1}J_{C,F}$ = 274.7 Hz, CF_3), 125.6, 129.1 (CH_{Ar}), 135.0 (q, $^{2}J_{C,F}$ = 35.9 Hz, $\underline{C}CF_3$), 136.6 (C_{Ar}), 146.6 (CH_{Ar}), 151.3, 152.3 (C_{Ar}), 155.3 (C=O), 157.5 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.50 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 1650 (m), 1604 (m), 1595 (m), 1572 (m), 1482 (m), 1459 (m), 1406 (m), 1360 (m), 1309 (w), 1273 (m), 1262 (m), 1185 (m), 1144 (s), 1097 (m), 983 (m), 749 (s). MS (EI, 70 eV): *m/z* (%) = 346 (20) [M^++1], 345 (100) [M^+], 325 (11), 316 (26), 77 (19). HRMS (ESI): calcd for $C_{17}H_{11}F_3N_3O_2$ ([M+1]$^+$) 346.0798, found 346.0799. Anal. Calcd for $C_{17}H_{10}F_3N_3O_2$: C, 59.14; H, 2.92; N, 12.17. Found: C, 59.25; H, 2.78; N, 12.02.

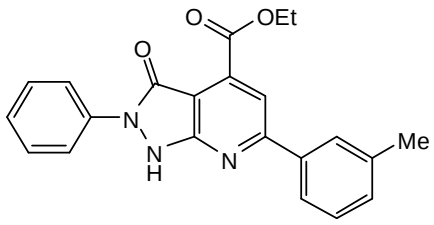
4-(Chlorodifluoromethyl)-6-(4-chlorophenyl)-2-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2r)



Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (113 mg, 1 mmol) and 4-chloro-1-(4-chlorophenyl)-4,4-difluorobutane-1,3-dione **6j** (320 mg, 1.2 mmol), **2r** was isolated via crystallization from benzene as yellow crystals (330 mg, 96%); mp 273-275 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.47 (s, 3H, CH_3), 6.89 (s, 1H, H-5), 7.50 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar), 8.07 (d, $^{3}J_{H,H}$ = 8.6 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 31.9 (CH_3), 94.5 (C-3a), 99.3 (t, $^{3}J_{C,F}$ = 6.6 Hz, C-5), 124.9 (t, $^{1}J_{C,F}$ = 291.1 Hz, $CClF_2$), 128.5, 128.6 (CH_{Ar}), 133.6, 138.5 (C_{Ar}), 139.4 (t, $^{2}J_{C,F}$ = 27.8 Hz, $\underline{C}CClF_2$), 153.8 (C_{Ar}), 155.5 (C=O), 156.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -48.67 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2916 (w), 2766 (w), 1665 (w), 1631 (m), 1584 (s), 1427 (m), 1402 (m), 1360 (m), 1276 (m), 1206 (m), 1144 (m), 1090 (s), 916 (m), 833 (s). MS (EI, 70 eV): *m/z* (%) = 345 (13) [M^++1], 344 (100) [M^+], 225 (31), 135 (33), 91 (11), 77 (69), 51 (12), 43 (38). HRMS (ESI): calcd for $C_{14}H_{10}Cl_2F_2N_3O$ ([M+1]$^+$) 344.0098, found 344.0094. Anal. Calcd for $C_{14}H_9Cl_2F_2N_3O$: C, 48.86; H, 2.64; N, 12.21. Found: C, 49.02; H, 2.55; N, 11.93.

Ethyl 3-oxo-2-phenyl-6-*m*-tolyl-2,3-dihydro-1*H*-pyrazolo[3,4-b]pyridine-4-carboxylate (2s)

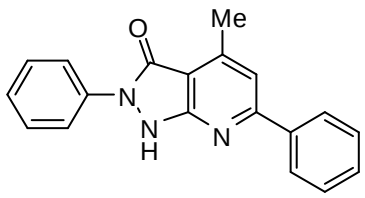


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and ethyl 2,4-dioxo-4-m-tolylbutanoate **6k** (281 mg, 1.2 mmol), **2s** was isolated by column chromatography as brown solid (231 mg, 65%); mp 174-176 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.38 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, $OCH_2\underline{CH_3}$), 2.42 (s, 3H, CH_3), 4.43 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, $O\underline{CH_2}CH_3$), 7.29 (t, $^{3}J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.36 (d, $^{3}J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.44 (t, $^{3}J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.50-7.55 (m, 2H, Ar), 7.91 (d, $^{3}J_{H,H}$ = 7.9 Hz, 3H, Ar), 8.00 (d, $^{3}J_{H,H}$ = 7.9 Hz, 1H, Ar), 8.05 (s, 1H, H-5), 11.90 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 14.0 ($CH_2\underline{C}H_3$), 21.5 (CH_3), 61.9 (CH_2), 104.4 (C-3a), 112.5 (C-5), 119.7, 124.6, 125.4, 127.9, 128.9, 129.1, 131.3 (CH_{Ar}), 137.0, 138.3, 139.6, 140.0, 156.6 (C_{Ar}), 157.5 (C=O), 160.7 (C-7a), 164.9 ($\underline{C}O_2Et$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2979 (w), 1729 (w), 1682 (w), 1651 (m), 1581 (s), 1496 (m), 1371 (m), 1346 (m), 1260 (s), 1206 (m), 1156 (m), 1037 (m), 1022 (m), 752 (s), 684 (s). MS (EI, 70 eV): *m/z* (%) = 375 (3) [M^++2], 374 (24) [M^++1], 373 (100) [M^+], 327 (15), 301 (63), 272 (14), 77 (25). HRMS (ESI): calcd for

$C_{22}H_{20}N_3O_3$ ([M+1]$^+$) 374.1499, found 374.1504. Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25. Found: C, 70.86; H, 4.98; N, 11.08.

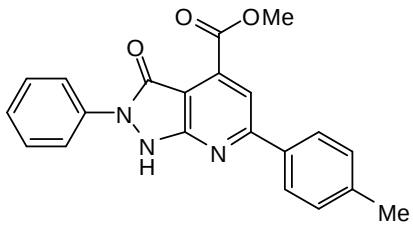
4-Methyl-2,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2t)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-phenylbutane-1,3-dione **6l** (194 mg, 1.2 mmol), **2t** was isolated by column chromatography as pink crystals (208 mg, 69%); mp 200-202 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d$_6$): 2.74 (s, 3H, CH_3), 7.27 (t, $^3J_{H,H}$ = 7.7 Hz, 1H, Ar), 7.49-7.60 (m, 6H, Ar), 7.96 (d, $^3J_{H,H}$ = 7.7 Hz, 2H, Ar), 8.16 (m, 2H, Ar), 11.44 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d$_6$): δ = 16.9 (CH_3), 108.0 (C-3a), 115.6 (C-5), 119.2, 124.8, 127.2, 128.8, 129.0, 130.0 (CH_{Ar}), 136.6, 136.7, 137.5, 155.4 (C_{Ar}), 159.3 (C=O), 160.3 (C-7a). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2994 (w), 2850 (w), 1638 (m), 1587 (m), 1496 (m), 1430 (m), 1389 (m), 1344 (m), 1300 (m), 1276 (m), 1208 (m), 1070 (w), 1025 (w), 911 (m), 856 (m), 769 (m), 748 (m), 681 (m). MS (EI, 70 eV): *m/z* (%) = 302 (22) [M$^+$+1], 301 (100) [M$^+$], 272 (37), 77 (11). HRMS (ESI): calcd for $C_{19}H_{16}N_3O$ ([M+1]$^+$) 302.1388, found 302.1291. Anal. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 76.84; H, 5.67; N, 12.97.

Methyl 3-oxo-2-phenyl-6-*p*-tolyl-2,3-dihydro-1H-pyrazolo[3,4-*b*]pyridine-4-carboxylate (2u)

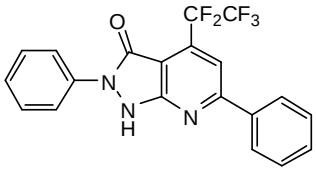


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and methyl 2,4-dioxo-4-p-tolylbutanoate **6m** (264 mg, 1.2 mmol), **2u** was isolated by column chromatography as brown solid (287 mg, 80%); mp 110-112 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.38 (s, 3H, CH_3), 3.95 (s, 3H, OCH_3), 7.28 (t, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.36 (2H, d, $^3J_{H,H}$ = 7.8 Hz, Ar), 7.49-7.54 (m, 2H, Ar), 7.89-7.92 (m, 3H, H-5, Ar), 8.09-8.12 (m, 2H, Ar), 11.93 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d$_6$): δ = 20.9 (CH_3), 52.8 (OCH_3), 104.3 (C-3a), 112.6, 119.7, 125.4, 127.3, 129.0, 129.6 (CH_{Ar}), 134.2, 137.0, 139.1, 140.6, 156.5 (C_{Ar}), 157.5 (C=O), 160.5 (C-7a), 165.3 ($\underline{C}O_2CH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3042 (br), 1732 (w), 1682 (w), 1651 (m), 1645 (m), 1582 (s), 1496 (m), 1435 (w), 1393 (w), 1371 (m), 1349 (m), 1300 (w), 1271 (m), 1240 (m), 1185 (m), 1174 (m), 1094 (w), 1034 (m), 821 (m), 751 (m), 688 (m), 676 (m). MS (EI, 70 eV): *m/z* (%) = 360 [M+1]$^+$ (35), 359 [M]$^+$ (100), 327 (30), 302 (30), 301 (99), 300 (22), 299 (87), 272 (31), 77 (56). HRMS

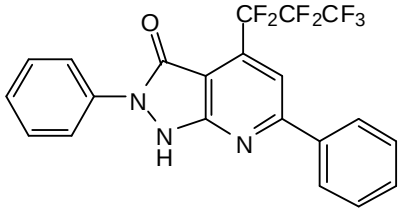
(ESI): calcd for $C_{21}H_{18}N_3O_3$ ([M+1]$^+$) 360.13427, found 360.13471. Anal. Calcd for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69. Found: C, 70.53; H, 4.69; N, 11.47.

4-(Perfluoroethyl)-2,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2v)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,5,5,5-pentafluoro-1-phenylpentane-1,3-dione **6n** (319 mg, 1.2 mmol), **2v** was isolated by column chromatography as yellow crystals (328 mg, 81%); mp 192-194 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.30 (t, $^3J_{H,H}$ = 7,4 Hz, 1H, Ph), 7.50-7.58 (m, 5H, Ph), 7.89-7.92 (m, 2H, Ph), 7.94 (s, 1H, H-5), 8.22-8.26 (m, 2H, Ph), 12.34 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 104.3 (C-3a), 112.3 (t, $^3J_{H,H}$ = 6.0 Hz, C-5), 120.2, 125.7, 127.6, 129.1, 129.1, 131.1 (CH_{Ar}), 134.6 (t, $^2J_{H,H}$ = 26.1 Hz, $\underline{C}CF_2CF_3$), 136.5, 136.6, 155.1 (C_{Ar}), 157.6 (C=O), 160.9 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -82.65 (s, 3F, CF_3), -110.55 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3066 (w), 1660 (w), 1594 (m), 1578 (m), 1488 (w), 1327 (m), 1272 (m), 1219 (s), 1186 (m), 1147 (s), 1048 (s), 727 (s), 687 (s). MS (EI, 70 eV): *m/z* (%) = 407 (3) [M$^+$+2], 406 (23) [M$^+$+1], 405 (100) [M$^+$], 376 (23), 77 (17). HRMS (ESI): calcd for $C_{20}H_{13}F_5N_3O$ ([M+1]$^+$) 406.0973, found 406.0973. Anal. Calcd for $C_{20}H_{12}F_5N_3O$: C, 59.27; H, 2.98; N, 10.37. Found: C, 59.42; H, 2.78; N, 10.68.

4-(Perfluoropropyl)-2,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2w)

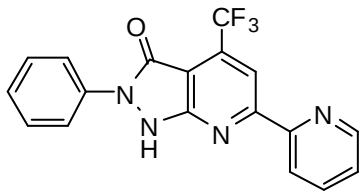


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,5,5,6,6,6-heptafluoro-1-phenylhexane-1,3-dione **6o** (379 mg, 1.2 mmol), **2w** was isolated by column chromatography as yellow crystals (346 mg, 76%); mp 201-203 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.31-7.36 (m, 1H, Ph), 7.52-7.58 (m, 5H, Ph), 7.89-7.95 (m, 4H, Ph, H-5), 8.28-8.31 (m, 1H, Ph), 12.42 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 108.5 (C-3a), 115.1 (t, $^3J_{H,H}$ = 6.0 Hz, C-5), 120.2, 125.8, 127.7, 128.1, 129.1, 131.0 (CH_{Ar}), 133.4 (t, $^2J_{H,H}$ = 26.1 Hz, $\underline{C}CF_2CF_3$), 136.5, 151.8, 155.1 (C_{Ar}), 156.7 (C=O), 160.9 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.61 (t, $^3J_{F,F}$ = 9.2 Hz, 3F, CF_3), -113.26 (q, $^3J_{F,F}$ = 9.2 Hz, 2F, CF_2), -125.48 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 3035 (w), 1659 (m), 1591 (m), 1487 (w), 1433 (w), 1393 (w), 1363 (m), 1273 (m), 1229 (s), 1201 (m), 1179 (s), 1145 (m), 1109 (s), 1003 (w), 916 (w), 853 (w), 808 (w), 754 (m), 730 (s), 685 (s), 637 (m). MS (EI, 70 eV): *m/z* (%) = 456 (23) [M$^+$+1], 455 (100) [M$^+$], 426 (16), 307 (8), 77 (27).

HRMS (ESI): calcd for $C_{21}H_{13}F_7N_3O$ ($[M+1]^+$) 456.09414, found 456.0947. Anal. Calcd for $C_{21}H_{12}F_7N_3O$: C, 55.39; H, 2.66; N, 9.23. Found: C, 55.54; H, 2.67; N, 9.30.

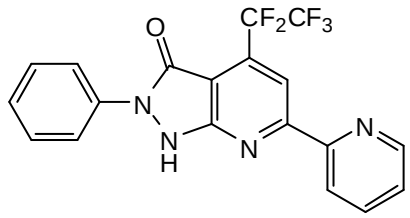
2-Phenyl-6-(pyridin-2-yl)-4-(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (2x)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,4-trifluoro-1-(pyridin-2-yl)butane-1,3-dione **6p** (261 mg, 1.2 mmol), **2x** was isolated via crystallization from ethanol as dark red crystals (328 mg, 92%); mp 250-252 ^oC.

IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3034 (w), 1603 (w), 1574 (w), 1538 (w), 1505 (w), 1480 (w), 1456 (w), 1373 (w), 1323 (w), 1273 (m), 1193 (m), 1121 (s), 1064 (m), 1036 (m), 1027 (m), 987 (m), 788 (m), 775 (m), 757 (m), 734 (m), 690 (s), 666 (s), 538 (m). MS (EI, 70 eV): *m/z* (%) = 357 (21) [M^++1], 356 (100) [M^+], 251 (34), 203 (21), 78 (18), 77 (46), 51 (17). HRMS (ESI): calcd for $C_{18}H_{12}F_3N_4O$ ($[M+1]^+$) 357.09577, found 357.09625. Anal. Calcd for $C_{18}H_{11}F_3N_4O$: C, 60.68; H, 3.11; N, 15.72. Found: C, 60.82; H, 3.15; N, 15.68.

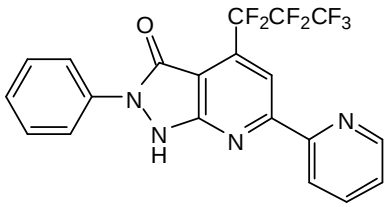
4-(Perfluoroethyl)-2-phenyl-6-(pyridin-2-yl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (2y)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,5,5,5-pentafluoro-1-(pyridin-2-yl)pentane-1,3-dione **6q** (321 mg, 1.2 mmol), **2y** was isolated via crystallization from ethanol as dark red crystals (386 mg, 95%); mp 302-303 ^oC.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.34-7.38 (m, 1H, Ar), 7.53-7.58 (m, 2H, Ar), 7.68 (br s, 1H, Ar), 7.96-8.01 (m, 3H, Ar), 8.11 (br s, 1H, Ar), 8.72 (br s, 1H, Ar), 8.86 (br s, 1H, Ar), 12.65 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -81.86 (s, 3F, CF_3), -115.43 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3083 (w), 3034 (w), 1605 (w), 1538 (w), 1504 (w), 1480 (m), 1459 (w), 1322 (m), 1206 (s), 1176 (m), 1147 (m), 1120 (m), 1085 (m), 1061 (m), 1033 (s), 1024 (s), 955 (m), 826 (m), 786 (s), 774 (s), 744 (s), 685 (s), 568 (m). MS (EI, 70 eV): *m/z* (%) = 407 (22) [M^++1], 406 (100) [M^+], 301 (27), 273 (15), 204 (12), 78 (19), 77 (52), 51 (16). HRMS (EI): calcd for $C_{19}H_{11}F_5N_4O$ ($[M]^+$) 406.08475, found 406.08423. Anal. Calcd for $C_{19}H_{11}F_5N_4O$: C, 56.16; H, 2.73; N, 13.79. Found: C, 56.37; H, 2.74; N, 13.75.

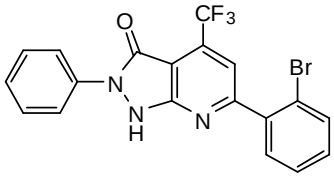
4-(Perfluoropropyl)-2-phenyl-6-(pyridin-2-yl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (2z)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 4,4,5,5,6,6,6-heptafluoro-1-(pyridin-2-yl)hexane-1,3-dione **6r** (381 mg, 1.2 mmol), **2z** was isolated via crystallization from ethanol as dark red crystals (443 mg, 97%); mp 275-277 °C.

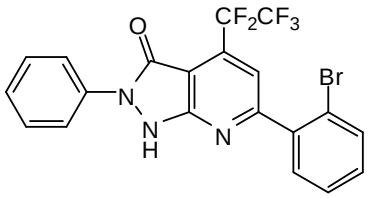
IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3076 (w), 3043 (w), 1603 (w), 1564 (w), 1538 (w), 1499 (w), 1480 (m), 1460 (w), 1334 (m), 1323 (m), 1203 (s), 1186 (m), 1113 (s), 1060 (m), 1038 (m), 996 (m), 903 (m), 812 (m), 790 (m), 775 (s), 759 (s), 745 (s), 733 (s), 686 (s), 667 (s), 589 (m). MS (EI, 70 eV): *m/z* (%) = 457 (29) [M^++1], 456 (100) [M^+], 351 (22), 323 (12), 204 (12), 78 (10), 77 (28), 51 (7). HRMS (ESI): calcd for $C_{20}H_{12}F_7N_4O$ ([M+1]$^+$) 457.08938, found 457.08992. Anal. Calcd for $C_{20}H_{11}F_7N_4O$: C, 52.64; H, 2.43; N, 12.28. Found: C, 52.74; H, 2.44; N, 12.27.

6-(2-Bromophenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2aa)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(2-bromophenyl)-4,4,4-trifluorobutane-1,3-dione **6s** (354 mg, 1.2 mmol), **2aa** was isolated by column chromatography as green crystals (395 mg, 91%); mp 192-194 °C. ^{1}H NMR (300 MHz, Aceton-d_6): δ = 7.30 (tt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.44-7.62 (m, 4H, Ar), 7.71 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, Ar), 7.76 (s, 1H, H-5), 7.82 (dd, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.97-8.02 (m, 2H, Ar), 10.81 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.01 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 1651 (m), 1591 (m), 1497 (m), 1434 (m), 1371 (m), 1311 (w), 1282 (m), 1267 (m), 1247 (m), 1184 (m), 1137 (s), 1023 (m), 981 (m), 886 (w), 748 (s), 719 (s), 685 (m). MS (EI, 70 eV): *m/z* (%) = 436 (20) [M^++1, ^{81}Br], 435 (100) [M^+, ^{81}Br], 434 (24) [M^++1, ^{79}Br], 433 (100) [M^+, ^{79}Br], 415 (13), 413 (12), 406 (28), 404 (28), 302 (11), 300 (12), 77 (80), 51 (18). HRMS (EI): calcd $C_{19}H_{11}BrF_3N_3O$ ([M]$^+$, ^{81}Br) 435.00116, found 435.00089. Anal. Calcd for $C_{19}H_{11}BrF_3N_3O$: C, 52.56; H, 2.55; N, 9.68. Found: C, 52.72; H, 2.56; N, 9.64.

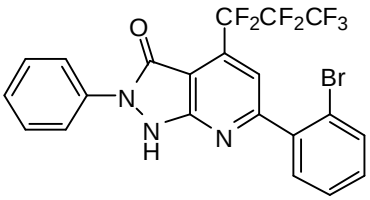
6-(2-Bromophenyl)-4-(perfluoroethyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ab)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(2-bromophenyl)-4,4,5,5,5-pentafluoropentane-1,3-dione **6t** (414 mg, 1.2 mmol), **2ab** was isolated by column chromatography as yellow crystals (426 mg, 88 %); mp 252-253 °C.

^{1}H NMR (250 MHz, Acetone-d_6): δ = 7.31 (tt, $^{3}J_{H,H}$ = 7.4 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.45-7.63 (m, 4H, Ar), 7.70-7.75 (m, 2H, Ar, H-5), 7.83 (dd, $^{3}J_{H,H}$ = 7.4 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.97-8.02 (m, 2H, Ar), 10.82 (s, 1H, NH). ^{13}C NMR (62.9 MHz, Acetone-d_6): δ = 107.0 (C-3a), 118.3 (t, $^{3}J_{H,H}$ = 8.2 Hz, C-5), 120.9 (CH_{Ar}), 121.9 (C_{Ar}), 126.6, 128.9, 129.9, 132.2, 132.6, 134.4 (CH_{Ar}), 135.4 (t, $^{2}J_{H,H}$ = 26.8 Hz, $\underline{C}CF_2CF_3$), 138.2, 140.5, 156.4 (C_{Ar}), 159.4 (C=O), 163.7 (C-7a). ^{19}F NMR (282 MHz, Acetone-d_6): δ = -83.12 (s, 3F, CF_3), -111.10 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3116 (w), 3093 (w), 1668 (m), 1693 (m), 1488 (w), 1426 (w), 1392 (w), 1358 (w), 1331 (w), 1274 (w), 1216 (m), 1185 (m), 1163 (m), 1148 (s), 1049 (s), 1026 (m), 950 (m), 869 (w), 808 (w), 754 (s), 729 (s), 708 (m), 688 (m), 629 (m). MS (EI, 70 eV): *m/z* (%) = 486 (23) [M^++1, ^{81}Br], 485 (97) [M^+, ^{81}Br], 484 (26) [M^++1, ^{79}Br], 483 (100) [M^+, ^{79}Br], 456 (23), 454 (24), 352 (9), 350 (8), 298 (9), 77 (75), 51 (14). HRMS (EI): calcd $C_{20}H_{11}BrF_5N_3O$ ([M]$^+$, ^{81}Br) 484.99797, found 484.99789. Anal. Calcd for $C_{20}H_{11}BrF_5N_3O$: C, 49.61; H, 2.29; N, 8.68. Found: C, 49.80; H, 2.30; N, 8.64.

6-(2-Bromophenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ac)

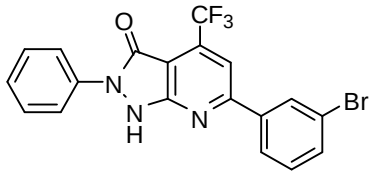


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(2-bromophenyl)-4,4,5,5,6,6,6-heptafluorohexane-1,3-dione **6u** (474 mg, 1.2 mmol), **2ac** was isolated by column chromatography as yellow crystals (422 mg, 79 %); mp 232-234 °C.

^{1}H NMR (250 MHz, Acetone-d_6): δ = 7.31 (tt, $^{3}J_{H,H}$ = 7.4 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.45-7.63 (m, 4H, Ar), 7.70-7.74 (m, 2H, Ar, H-5), 7.83 (dd, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.97-8.02 (m, 2H, Ar), 10.83 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 104.5 (C-3a), 116.6 (t, $^{3}J_{H,H}$ = 8.7 Hz, C-5), 120.5 (CH_{Ar}), 120.8 (C_{Ar}), 126.0, 128.1, 129.1, 131.5, 131.6, 133.3 (CH_{Ar}), 136.4, 139.0, 154.8 (C_{Ar}), 156.8 (C=O), 162.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.44 (t, $^{3}J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.68 (q, $^{3}J_{F,F}$ = 9.2 Hz, 2F, CF_2), -124.26 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 3019 (w), 1661 (m), 1593 (m), 1497 (w),

1487 (w), 1427 (w), 1392 (w), 1361 (m), 1342 (w), 1278 (m), 1224 (s), 1201 (m), 1186 (m), 1147 (m), 1107 (s), 1028 (m), 1001 (m), 913 (m), 854 (w), 792 (m), 753 (m), 736 (s), 711 (m), 689 (m), 637 (m). MS (EI, 70 eV): *m/z* (%) = 536 (23) [M^++1, ^{81}Br], 535 (100) [M^+, ^{81}Br], 534 (27) [M^++1, ^{79}Br], 533 (97) [M^+, ^{79}Br], 506 (15), 504 (15), 402 (8), 400 (9), 77 (78), 51 (13). HRMS (EI): calcd $C_{21}H_{11}BrF_7N_3O$ ([M]$^+$, ^{81}Br) 534.99478, found 534.99427. Anal. Calcd for $C_{21}H_{11}BrF_7N_3O$: C, 47.21; H, 2.08; N, 7.87. Found: C, 47.38; H, 2.12; N, 7.78.

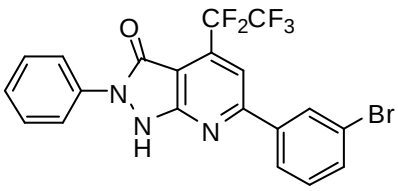
6-(3-Bromophenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ad)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(3-bromophenyl)-4,4,4-trifluorobutane-1,3-dione **6v** (354 mg, 1.2 mmol), **2ad** was isolated by column chromatography as yellow crystals (421 mg, 97%); mp 203-205 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.32 (tt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Ar), 7.51-7.57 (m, 3H, Ar), 7.77 (dq, $^3J_{H,H}$ = 7.9 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Ar), 7.88-7.92 (m, 2H, Ar), 8.09 (s, 1H, H-5), 8.28 (dq, $^3J_{H,H}$ = 7.9 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Ar), 8.46 (t, $^4J_{H,H}$ = 1.8 Hz, 1H, Ar), 12.33 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.00 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 1651 (m), 1604 (m), 1567 (w), 1488 (w), 1398 (w), 1365 (m), 1304 (w), 1278 (m), 1257 (s), 1184 (m), 1148 (s), 1138 (s), 986 (m), 872 (m), 783 (m), 755 (m), 741 (m), 722 (m), 688 (s), 665 (m), 634 (m). MS (EI, 70 eV): *m/z* (%) = 436 (21) [M^++1, ^{81}Br], 435 (98) [M^+, ^{81}Br], 434 (23) [M^++1, ^{79}Br], 433 (95) [M^+, ^{79}Br], 415 (11), 413 (11), 406 (25), 404 (26), 302 (13), 300 (11), 77 (100), 51 (22). HRMS (EI): calcd $C_{19}H_{11}BrF_3N_3O$ ([M]$^+$, ^{81}Br) 435.00116, found 435.00133. Anal. Calcd for $C_{19}H_{11}BrF_3N_3O$: C, 52.56; H, 2.55; N, 9.68. Found: C, 52.68; H, 2.57; N, 9.62.

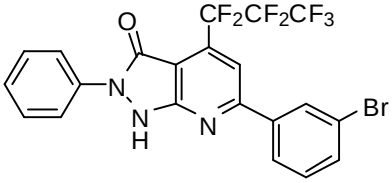
6-(3-Bromophenyl)-4-(perfluoroethyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ae)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(3-bromophenyl)-4,4,5,5,5-pentafluoropentane-1,3-dione **6w** (414 mg, 1.2 mmol), **2ae** was isolated by column chromatography as green crystals (441 mg, 91%); mp 248-249 ^{o}C.

^{1}H NMR (250 MHz, Acetone-d_6): δ = 7.30 (tt, $^{3}J_{H,H}$ = 7.4 Hz, $^{4}J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.49-7.58 (m, 3H, Ar), 7.76 (ddd, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.8 Hz, $^{4}J_{H,H}$ = 1.0 Hz, 1H, Ar), 7.97-8.02 (m, 2H, Ar), 8.09 (s, 1H, H-5), 8.30 (ddd, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.8 Hz, $^{4}J_{H,H}$ = 1.0 Hz, 1H, Ar), 8.48 (t, $^{4}J_{H,H}$ = 1.8 Hz, 1H, Ar), 10.75 (s, 1H, NH). ^{13}C NMR (62.9 MHz, Acetone-d_6): δ = 107.5 (C-3a), 114.1 (t, $^{3}J_{H,H}$ = 8.2 Hz, C-5), 120.8 (CH_{Ar}), 123.7 (C_{Ar}), 126.5, 127.5, 129.9, 131.4, 131.9, 134.6 (CH_{Ar}), 136.8 (t, $^{2}J_{H,H}$ = 26.3 Hz, $\underline{C}CF_2CF_3$), 138.2, 140.2, 156.5 (C_{Ar}), 159.7 (C=O), 160.8 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -81.88 (s, 3F, CF_3), -114.35 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3064 (w), 1658 (m), 1594 (m), 1564 (w), 1494 (w), 1424 (w), 1401 (w), 1355 (w), 1332 (w), 1301 (w), 1276 (m), 1220 (m), 1209 (m), 1189 (m), 1163 (m), 1149 (s), 1098 (w), 1049 (s), 957 (m), 866 (w), 793 (w), 753 (m), 732 (m), 687 (s), 637 (m). MS (EI, 70 eV): *m/z* (%) = 486 (22) [M^++1, ^{81}Br], 485 (100) [M^+, ^{81}Br], 484 (25) [M^++1, ^{79}Br], 483 (99) [M^+, ^{79}Br], 456 (20), 454 (20), 298 (12), 77 (91), 51 (16). HRMS (EI): calcd $C_{20}H_{11}BrF_5N_3O$ ([M]$^+$, ^{81}Br) 484.99797, found 484.99776. Anal. Calcd for $C_{20}H_{11}BrF_5N_3O$: C, 49.61; H, 2.29; N, 8.68, Found: C, 49.79; H, 2.34; N, 8.67.

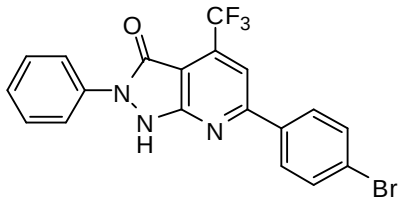
6-(3-Bromophenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2af)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(3-bromophenyl)-4,4,5,5,6,6,6-heptafluorohexane-1,3-dione **6x** (474 mg, 1.2 mmol), **2af** was isolated by column chromatography as yellow crystals (502 mg, 94%); mp 263-264 °C.

IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3077 (w), 3019 (w), 1659 (m), 1597 (w), 1567 (w), 1488 (w), 1423 (w), 1401 (w), 1359 (w), 1339 (w), 1305 (w), 1274 (w), 1229 (s), 1201 (m), 1184 (m), 1147 (m), 1113 (m), 1074 (w), 1006 (w), 923 (m), 855 (w), 811 (w), 755 (m), 734 (s), 706 (m), 684 (s), 662 (m), 640 (m). MS (EI, 70 eV): *m/z* (%) = 536 (22) [M^++1, ^{81}Br], 535 (100) [M^+, ^{81}Br], 534 (27) [M^++1, ^{79}Br], 533 (100) [M^+, ^{79}Br], 506 (14), 504 (14), 402 (8), 400 (9), 77 (81), 51 (13). HRMS (EI): calcd $C_{21}H_{11}BrF_7N_3O$ ([M]$^+$, ^{81}Br) 534.99478, found 534.99393. Anal. Calcd for $C_{21}H_{11}BrF_7N_3O$: C, 47.21; H, 2.08; N, 7.87. Found: C, 47.31; H, 2.10; N, 7.86.

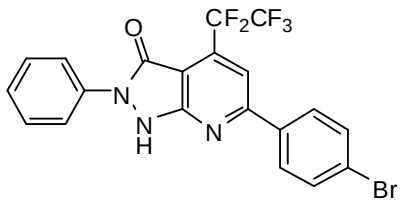
6-(4-Bromophenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ag)



Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(4-bromophenyl)-4,4,4-trifluorobutane-1,3-dione **6y** (354 mg, 1.2 mmol), **2ag** was isolated by column chromatography as green crystals (343 mg, 79%); mp 203-205 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.32 (t, $^3J_{H,H}$ = 7,1 Hz, 1H, Ar), 7.54 (t, $^3J_{H,H}$ = 7,7 Hz, 2H, Ar), 7.79 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar), 7.90 (d, $^3J_{H,H}$ = 7,7 Hz, 2H, Ar), 8.05 (s, 1H, H-5), 8.24 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ph), 12.35 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.06 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3043 (br), 2978 (w), 1668 (w), 1650 (w), 1645 (w), 1601 (w), 1584 (m), 1496 (w), 1393 (w), 1369 (m), 1274 (m), 1260 (w), 1184 (w), 1157 (m), 1140 (m), 1071 (w), 1007 (w), 981 (w), 950 (m), 829 (m), 752 (m), 715 (m), 649 (m). MS (EI, 70 eV): *m/z* (%) = 436 (21) [M^++1, ^{81}Br], 435 (98) [M^+, ^{81}Br], 434 (24) [M^++1, ^{79}Br], 433 (100) [M^+, ^{79}Br], 415 (12), 413 (11), 406 (24), 404 (25), 302 (11), 300 (11), 77 (99), 51 (21). HRMS (EI): calcd $C_{19}H_{12}BrF_3N_3O$ ([M]$^+$, ^{81}Br) 436.00919, found 436.00914. Anal. Calcd for $C_{19}H_{11}BrF_3N_3O$: C, 52.56; H, 2.55; N, 9.68. Found: C, 52.74; H, 2.56; N, 9.94.

6-(4-Bromophenyl)-4-(perfluoroethyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ah)

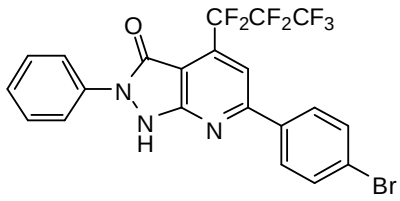


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(4-bromophenyl)-4,4,5,5,5-pentafluoropentane-1,3-dione **6z** (414 mg, 1.2 mmol), **2ah** was isolated by column chromatography as yellow crystals (387 mg, 80%); mp 248-249 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.32 (t, $^3J_{H,H}$ = 7,4 Hz, 1H, Ar), 7.51-7.57 (m, 2H, Ar), 7.76-7.80 (m, 2H, Ar), 7.88-7.91 (m, 2H, Ar), 7.99 (s, 1H, H-5), 8.20-8.24 (m, 2H, Ar), 12.38 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 104.5 (C-3a), 112.2 (C-5), 120.2 (CH_{Ar}), 124.9 (C_{Ar}), 125.8, 129.1, 129.7, 132.1 (CH_{Ar}), 134.8 (t, $^2J_{C,F}$ = 27.0 Hz, CCF_2), 135.7, 136.6, 155.0 (C_{Ar}), 157.4 (C=O), 159.8 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -82.60 (s, 3F, CF_3), -110.48 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3021 (w), 2921 (w), 1651 (m), 1594 (m), 1584 (m), 1496 (w), 1431 (w), 1395 (w), 1361 (w), 1328 (w), 1274 (m), 1219 (m), 1190 (m), 1149 (s), 1048 (s), 1008 (m), 950 (m), 831 (m), 752 (m), 732 (s), 688 (m). MS (EI, 70 eV): *m/z* (%) = 486 (21) [M^++1, ^{81}Br], 485 (97) [M^+, ^{81}Br], 484 (25) [M^++1, ^{79}Br], 483 (100) [M^+, ^{79}Br], 456 (20), 454 (21), 298 (12), 77 (91), 51 (17). HRMS (EI): calcd $C_{20}H_{11}BrF_5N_3O$

([M]$^+$, ^{81}Br) 484.99797, found 484.99718. Anal. Calcd for $C_{20}H_{11}BrF_5N_3O$: C, 49.61; H, 2.29; N, 8.68. Found: C, 49.80; H, 2.30; N, 8.65.

6-(4-Bromophenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (2ai)



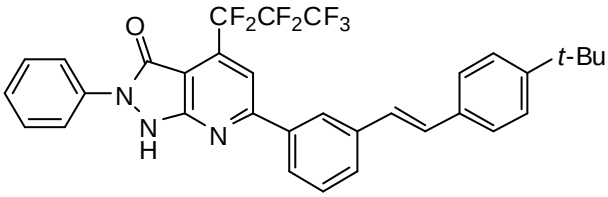
Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (175 mg, 1 mmol) and 1-(4-bromophenyl)-4,4,5,5,6,6,6-heptafluorohexane-1,3-dione **6aa** (474 mg, 1.2 mmol), **2ai** was isolated by column chromatography as yellow crystals (454 mg, 85%); mp 288-289 ^{o}C.

^{1}H NMR (250 MHz, Acetone-d_6): δ = 7.30 (tt, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.1 Hz, 1H, Ar), 7.48-7.57 (m, 2H, Ar), 7.75-7.80 (m, 2H, Ar), 7.97-8.02 (m, 2H, Ar), 8.04 (s, 1H, H-5), 8.23-8.29 (m, 2H, Ar), 10.75 (s, 1H, NH). ^{13}C NMR (62.9 MHz, Acetone-d_6): δ = 107.5 (C-3a), 114.1 (t, $^3J_{H,H}$ = 8.2 Hz, C-5), 120.8 (CH_{Ar}), 126.1 (C_{Ar}), 126.5, 129.9, 130.5, 133.1 (CH_{Ar}), 137.1, 138.3, 156.6 (C_{Ar}), 159.8 (C=O), 161.3 (C-7a). ^{19}F NMR (282 MHz, Acetone-d_6): δ = -81.21 (t, $^3J_{F,F}$ = 9.2 Hz, 3F, CF_3), -105.24 (q, $^3J_{F,F}$ = 9.2 Hz, 2F, CF_2), -125.26 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3043 (br), 1660 (m), 1585 (m), 1497 (w), 1487 (w), 1434 (w), 1393 (w), 1363 (m), 1341 (w), 1272 (m), 1226 (s), 1203 (m), 1181 (m), 1148 (m), 1112 (m), 1072 (w), 1003 (m), 916 (w), 832 (m), 807 (m), 754 (m), 734 (s), 686 (m), 623 (m). MS (EI, 70 eV): *m/z* (%) = 536 (23) [M$^+$+1, ^{81}Br], 535 (100) [M$^+$, ^{81}Br], 534 (28) [M$^+$+1, ^{79}Br], 533 (99) [M$^+$, ^{79}Br], 506 (13), 504 (12), 77 (69), 51 (10). HRMS (EI): calcd $C_{21}H_{11}BrF_7N_3O$ ([M]$^+$, ^{81}Br) 534.99478, found 534.99443. Anal. Calcd for $C_{21}H_{11}BrF_7N_3O$: C, 47.21; H, 2.08; N, 7.87. Found: C, 47.35; H, 2.09; N, 7.86.

A.2.2. General procedure for synthesis of compounds 9

Under argon atmosphere, 4-*tert*-butylstyrene (0.55 ml, 3 mmol), 1H-pyrazolo[3,4-b]pyridin-3-one **2** (1 mmol), triethylamine (0.56 ml, 4 mmol) and $PdCl_2(PPh_3)_2$ (28 mg, 0.04 mol) were placed into a pressure tube and 4mL of dry DMF was added. Once the pressure tube was sealed, the mixture was heated at 140 ^{o}C for 6 – 20h (controlled by TLC). Then the solution was evaporated under reduced pressure and subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

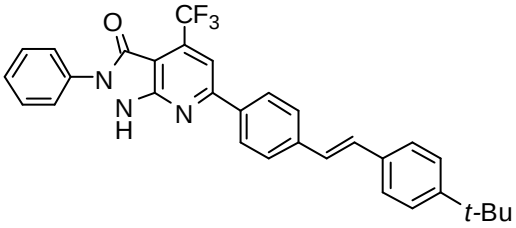
(*E*)-6-(3-(4-Tert-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (9a)



Starting from **2af** (534 mg, 1 mmol) **9a** was isolated by column chromatography as green crystals (472 mg, 77%); mp 250-252 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.30 (s, 9H, CH_3), 7.32 (t, $^{3}J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.38-7.44 (m, 4H, Ar), 7.51-7.62 (m, 5H, Ar), 7.85 (d, $^{3}J_{H,H}$ = 8.0 Hz, 1H, =CH), 7.90-7.93 (m, 2H, Ar), 8.04 (s, 1H, H-5), 8.16 (d, $^{3}J_{H,H}$ = 8.0 Hz, 1H, =CH), 8.43 (s, 1H, Ar), 12.36 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.34 (t, $^{3}J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.41 (q, $^{3}J_{F,F}$ = 9.2 Hz, 2F, CF_2), -124.05 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3029 (w), 2959 (w), 1658 (m), 1595 (m), 1497 (w), 1433 (w), 1394 (w), 1362 (m), 1274 (m), 1228 (s), 1204 (m), 1183 (m), 1147 (m), 1113 (s), 1008 (w), 963 (w), 940 (w), 846 (w), 817 (m), 755 (m), 733 (s), 684 (s), 566 (w). MS (EI, 70 eV): *m/z* (%) = 614 (31) [M^{+}+1], 613 (97) [M^{+}], 599 (33), 598 (100), 557 (14), 299 (14), 77 (9), 44 (8). HRMS (ESI): calcd $C_{33}H_{27}F_7N_3O$ ([M+1]$^{+}$) 614.20369, found 614.20398. Anal. Calcd for $C_{33}H_{26}F_7N_3O$: C, 64.60; H, 4.27; N, 6.85. Found: C, 64.87; H, 4.29; N, 6.82.

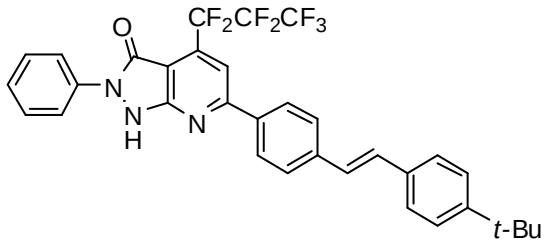
(*E*)-6-(4-(4-Tert-butylstyryl)phenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (9b)



Starting from **2ag** (434 mg, 1 mmol) **9b** was isolated by column chromatography as yellow crystals (416 mg, 81%); mp 270-272 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.29 (s, 9H, CH_3), 7.26-7.33 (m, 2H, Ar), 7.38-7.43 (m, 3H, Ar), 7.51-7.59 (m, 4H, Ar), 7.77-7.80 (m, 2H, Ar), 7.90-7.92 (m, 2H, Ar, =CH), 8.05 (s, 1H, H-5), 8.28-8.31 (m, 2H, Ar, =CH), 12.26 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.10 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3077 (w), 2959 (w), 1646 (m), 1593 (m), 1496 (w), 1407 (m), 1374 (m), 1276 (m), 1260 (m), 1168 (m), 1139 (s), 978 (w), 964 (m), 871 (w), 838 (s), 748 (s), 711 (m), 687 (m), 560 (m). MS (EI, 70 eV): *m/z* (%) = 514 (46) [M^{+}+1], 513 (95) [M^{+}], 499 (49), 498 (100), 367 (16), 249 (19), 169 (11), 77 (12), 69 (11), 44 (67), 43 (14). HRMS (ESI): calcd $C_{31}H_{27}F_3N_3O$ ([M+1]$^{+}$) 514.21007, found 514.20972. Anal. Calcd for $C_{31}H_{26}F_3N_3O$: C, 72.50; H, 5.10; N, 8.18. Found: C, 72.78; H, 5.12; N, 8.14.

(*E*)-6-(4-(4-Tert-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (9c)



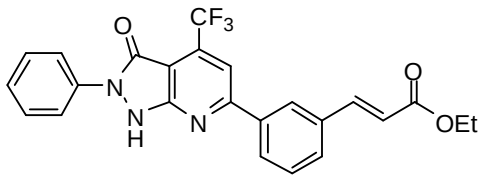
Starting from **2ai** (534 mg, 1 mmol) **9c** was isolated by column chromatography as yellow crystals (515 mg, 84%); mp 203-205 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.30 (s, 9H, CH_3), 7.28-7.33 (m, 2H, Ar), 7.39-7.44 (m, 3H, Ar), 7.51-7.60 (m, 4H, Ar, =CH), 7.90-7.92 (m, 2H, Ar), 7.99 (s, 1H, H-5), 8.29-8.32 (m, 2H, Ar, =CH), 12.29 (s, 1H, NH). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.35 (t, $^{3}J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.49 (q, $^{3}J_{F,F}$ = 9.2 Hz, 2F, CF_2), -124.11 (t, $^{3}J_{F,F}$ = 21.5 Hz, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3029 (w), 2959 (w), 1658 (m), 1595 (m), 1497 (w), 1433 (w), 1394 (w), 1362 (m), 1274 (m), 1228 (s), 1204 (m), 1183 (m), 1147 (m), 1113 (s), 1008 (w), 963 (w), 940 (w), 846 (w), 817 (m), 755 (m), 733 (s), 684 (s), 566 (w). MS (EI, 70 eV): *m/z* (%) = 614 (38) [M^{+}+1], 613 (100) [M^{+}], 599 (28), 598 (97), 557 (21), 299 (14), 77 (19), 44 (17). HRMS (ESI): calcd $C_{33}H_{27}F_7N_3O$ ([M+1]$^{+}$) 614.20369, found 614.20382. Anal. Calcd for $C_{33}H_{26}F_7N_3O$: C, 64.60; H, 4.27; N, 6.85. Found: C, 64.39; H, 4.25; N, 6.83.

A.2.3. General procedure for synthesis of compounds 11-13, 15

Under argon atmosphere, appropriate alkene, 1H-pyrazolo[3,4-b]pyridin-3-one **2** (1 mmol), triethylamine (0.56 ml, 4 mmol) and $PdCl_2(PPh_3)_2$ (28 mg, 0.04 mol) were placed into a pressure tube and 4mL of dry DMF was added. Once the pressure tube was sealed, the mixture was heated at 80-100 ^{o}C for 6 – 20h (controlled by TLC). Then the solution was evaporated under reduced pressure and subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

(*E*)-Ethyl 3-(3-(3-oxo-2-phenyl-4-(trifluoromethyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)phenyl)acrylate (11a)

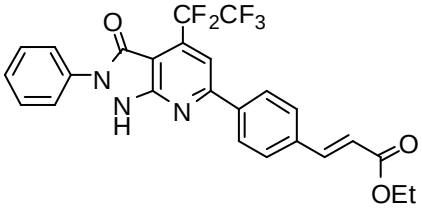


Starting from ethylacrylate (120 mg, 1.2 mmol) and **2ad** (434 mg, 1 mmol) **11a** was isolated by column chromatography as yellow crystals (190 mg, 42%); mp 236-237 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.28 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_3), 4.22 (q, $^{3}J_{H,H}$ = 7.1 Hz, 2H, OCH_2), 6.86 (d, $^{3}J_{H,H}$ = 16.1 Hz, 1H, =CH), 7.29-7.34 (m, 1H, Ar), 7.51-7.57 (m, 2H, Ar), 7.62 (t, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.79 (d, $^{3}J_{H,H}$ = 16.1 Hz, 1H, =CH), 7.89-7.92 (m, 3H, Ar),

8.18 (s, 1H, H-5), 8.31 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.59 (br s, 1H, Ar), 12.31 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 14.2 (CH_3), 60.2 (OCH_2), 103.4 (C-3a), 111.1 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 119.3 (=CH), 120.1 (CH_{Ar}), 122.0 (q, $^{1}J_{C,F}$ = 274.4 Hz, CF_3), 125.8, 127.5, 129.1, 129.3, 129.7, 130.6 (CH_{Ar}), 135.0 (C_{Ar}), 135.8 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 136.6, 137.4 (C_{Ar}), 143.7 (=CH), 155.4 (C_{Ar}), 157.5 (NC=O), 160.6 (C-7a), 166.2 ($\underline{C}O_2Et$). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -60.94 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3212 (br w), 1687 (m), 1683 (m), 1634 (w), 1594 (w), 1499 (w), 1440 (w), 1393 (w), 1369 (m), 1315 (w), 1299 (w), 1259 (w), 1202 (m), 1146 (s), 1083 (w), 1033 (w), 993 (w), 864 (w), 803 (w), 754 (m), 709 (m), 687 (m). MS (EI, 70 eV): *m/z* (%) = 454 (69) [M^++1], 453 (100) [M^+], 425 (18), 408 (62), 407 (87), 379 (20), 378 (77), 204 (17), 77 (51), 44 (11). HRMS (ESI): calcd $C_{24}H_{18}F_3N_3O_3$ ([M]$^+$) 453.12948, found 453.12914. Anal. Calcd for $C_{24}H_{18}F_3N_3O_3$: C, 63.57; H, 4.00; N, 12.57. Found: C, 63.84; H, 4.12; N, 7.63.

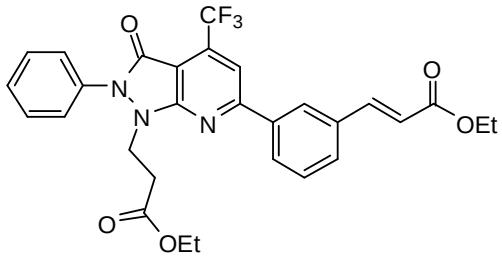
***(E)*-Ethyl 3-(4-(3-oxo-4-(perfluoroethyl)-2-phenyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)phenyl)acrylate (11b)**



Starting from ethylacrylate (120 mg, 1.2 mmol) and **2ah** (484 mg, 1 mmol) **11b** was isolated by column chromatography as yellow crystals (171 mg, 34%), mp 224-225 °C.

^{1}H NMR (300 MHz, DMSO-d_6): 1.38 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_3), 4.32 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, OCH_2), 6.58 (d, $^{3}J_{H,H}$ = 15.9 Hz, 1H, =CH), 7.35-7.41 (m, 1H, Ar), 7.51-7.61 (m, 4H, Ar), 7.65-7.88 (m, 4H, Ar, =CH), 8.20-8.23 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 14.7 (CH_3), 61.3 (OCH_2), 106.8 (C-3a), 114.0 (t, $^{3}J_{C,F}$ = 7.8 Hz, C-5), 120.5 (=CH), 124.6, 127.7, 128.6, 129.0, 129.7 (CH_{Ar}), 134.7 (C_{Ar}), 137.3 (t, $^{2}J_{C,F}$ = 27.2 Hz, $\underline{C}CF_3$), 137.5, 138.5 (C_{Ar}), 143.5 (=CH), 158.0 (C_{Ar}), 161.0 (NC=O), 161.3 (C-7a), 167.0 ($\underline{C}O_2Et$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -83.19 (q, $^{3}J_{F,F}$ = 3.1 Hz, 3F, CF_3), -111.77 (q, $^{3}J_{F,F}$ = 3.1 Hz, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 504 (18) [M^++1], 503 (69) [M^+], 460 (23), 459 (100), 77 (25). HRMS (ESI): calcd $C_{25}H_{19}F_5N_3O_3$ ([M+1]$^+$) 504.13258, found 504.13252. Anal. Calcd for $C_{25}H_{18}F_5N_3O_3$: C, 59.65; H, 3.60; N, 8.35. Found: C, 59.47; H, 3.31; N, 8.67.

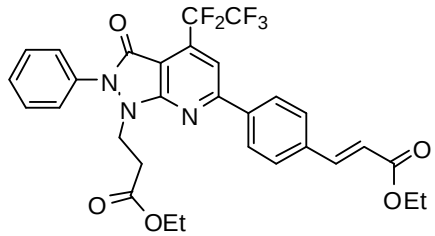
(*E*)-Ethyl 3-(2-(1-(3-ethoxy-3-oxopropyl)-3-oxo-2-phenyl-4-(trifluoromethyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)phenyl)acrylate (12a)



Starting from ethylacrylate (120 mg, 1.2 mmol) and **2ad** (434 mg, 1 mmol) **12a** was isolated by column chromatography as yellow solid (100 mg, 18%), mp 58-60 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.95 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_3), 1.29 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_3), 2.40 (t, $^{3}J_{H,H}$ = 6.6 Hz, 2H, $NCH_2\underline{CH_2}$), 3.77 (q, $^{3}J_{H,H}$ = 7.1 Hz, 2H, OCH_2), 4.23 (q, $^{3}J_{H,H}$ = 7.1 Hz, 2H, OCH_2), 4.33 (t, $^{3}J_{H,H}$ = 6.6 Hz, 2H, NCH_2), 6.90 (d, $^{3}J_{H,H}$ = 16.1 Hz, 1H, =CH), 7.40-7.46 (m, 1H, Ar), 7.56-7.60 (m, 4H, Ar), 7.65 (t, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.81 (d, $^{3}J_{H,H}$ = 16.1 Hz, 1H, =CH), 7.95 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.28 (s, 1H, H-5), 8.39 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.67 (br s, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.6, 14.2 (CH_3), 30.4, 43.8 (CH_2), 60.1, 60.2 (OCH_2), 104.2 (C-3a), 112.1 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 119.4 (=CH), 121.8 (q, $^{1}J_{C,F}$ = 275.1 Hz, CF_3), 124.5, 127.4, 127.7, 129.3, 129.6, 129.7, 130.9 (CH_{Ar}), 134.1, 135.0 (C_{Ar}), 135.5 (q, $^{2}J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 137.1 (C_{Ar}), 143.7 (=CH), 157.3 (C_{Ar}), 160.1 (NC=O), 161.0 (C-7a), 166.2, 170.4 ($\underline{C}O_2Et$). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.03 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2980 (w), 1704 (m), 1699 (m), 1639 (w), 1590 (m), 1487 (w), 1461 (w), 1446 (w), 1417 (w), 1368 (m), 1311 (m), 1260 (m), 1140 (s), 1032 (m), 980 (m), 862 (w), 799 (m), 756 (m), 713 (m), 690 (m), 661 (w). MS (EI, 70 eV): *m/z* (%) = 554 (24) [M^++1], 553 (76) [M^+], 508 (10), 467 (29), 466 (100), 77 (27). HRMS (EI): calcd $C_{29}H_{26}F_3N_3O_5$ ([M]$^+$) 553.18191, found 553.18178. Anal. Calcd for $C_{29}H_{26}F_3N_3O_5$: C, 62.93; H, 4.73; N, 7.59. Found: C, 62.78; H, 4.71; N, 7.62.

(*E*)-Ethyl 3-(4-(1-(3-ethoxy-3-oxopropyl)-3-oxo-4-(perfluoroethyl)-2-phenyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)phenyl)acrylate (12b)

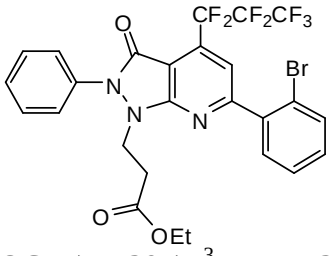


Starting from ethylacrylate (120 mg, 1.2 mmol) and **2ah** (484 mg, 1 mmol) **12c** was isolated by column chromatography as yellow oil (145 mg, 24%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_3), 1.36 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_3), 2.38 (t, $^{3}J_{H,H}$ = 7.3 Hz, 2H, $NCH_2\underline{CH_2}$), 3.95 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, OCH_2), 4.30 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, OCH_2), 4.42 (t, $^{3}J_{H,H}$ = 7.3 Hz, 2H, NCH_2), 6.56 (d, $^{3}J_{H,H}$ = 15.9 Hz, 1H, =CH), 7.33-7.39 (m, 1H, Ar), 7.49-7.59 (m, 4H, Ar), 7.63-7.86 (m, 4H, Ar, =CH), 8.18-8.21 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0, 14.5 (CH_3), 30.5, 44.1 (CH_2), 60.9, 61.1 (OCH_2), 106.6 (C-3a), 113.8 (t, $^{3}J_{C,F}$ = 7.8 Hz, C-5), 120.3 (=CH), 124.4, 127.5, 128.4, 128.8, 129.5 (CH_{Ar}),

134.5 (C_{Ar}), 137.1 (t, $^{2}J_{C,F}$ = 27.0 Hz, $\underline{C}CF_3$), 137.3, 138.3 (C_{Ar}), 143.3 (=CH), 157.8 (C_{Ar}), 160.8 (NC=O), 161.1 (C-7a), 166.8, 170.6 ($\underline{C}O_2Et$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -83.19 (q, $^{3}J_{F,F}$ = 3.1 Hz, 3F, CF_3), -111.77 (q, $^{3}J_{F,F}$ = 3.1 Hz, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3212 (w), 1690 (m), 1683 (m), 1634 (w), 1594 (w), 1499 (w), 1440 (w), 1393 (w), 1371 (m), 1315 (w), 1301 (w), 1259 (w), 1202 (m), 1151 (s), 1083 (w), 1005 (w), 862 (w), 754 (m), 709 (m). MS (EI, 70 eV): *m/z* (%) = 604 (22) [M^++1], 603 (84) [M^+], 517 (30), 516 (100), 503 (13), 77 (18). HRMS (ESI): calcd $C_{30}H_{27}F_5N_3O_5$ ([M+1]$^+$) 604.18654, found 604.18637. Anal. Calcd for $C_{30}H_{26}F_5N_3O_5$: C, 59.70; H, 4.34; N, 6.96. Found: C, 59.58; H, 4.36; N, 6.99.

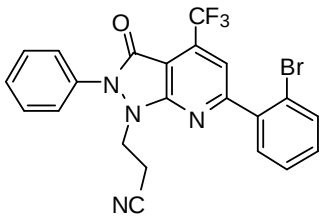
Ethyl 3-(6-(2-bromophenyl)-3-oxo-4-(perfluoropropyl)-2-phenyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)propanoate (13)



Starting from ethylacrylate (120 mg, 1.2 mmol) and **2ad** (484 mg, 1 mmol) **13** was isolated by column chromatography as yellow oil (444 mg, 70%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_3), 2.39 (t, $^{3}J_{H,H}$ = 7.3 Hz, 2H, $NCH_2\underline{CH_2}$), 3.96 (q, $^{3}J_{H,H}$ = 7.2 Hz, 2H, OCH_2), 4.39 (t, $^{3}J_{H,H}$ = 7.3 Hz, 2H, NCH_2), 7.34-7.41 (m, 2H, Ar), 7.48-7.59 (m, 5H, Ar), 7.66 (dd, $^{3}J_{H,H}$ = 7.7 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 1H, Ar), 7.70 (s, 1H, H-5), 7.76 (dd, $^{3}J_{H,H}$ = 7.7 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.1 (CH_3), 30.6, 44.1 (CH_2), 61.0 (OCH_2), 106.9 (C-3a), 118.6 (t, $^{3}J_{C,F}$ = 8.5 Hz, C-5), 121.8 (C_{Ar}), 124.5, 127.6, 128.0, 129.6, 131.3, 131.8, 134.1 (CH_{Ar}), 134.4 (C_{Ar}), 136.1 (t, $^{2}J_{C,F}$ = 27.0 Hz, $\underline{C}CF_2$), 139.2, 157.9 (C_{Ar}), 160.4 (NC=O), 163.1 (C-7a), 170.5 ($\underline{C}O_2Et$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.35 (t, $^{3}J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.49 (q, $^{3}J_{F,F}$ = 9.2 Hz, 2F, CF_2), -124.11 (t, $^{3}J_{F,F}$ = 21.5 Hz, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 636 (14) [M^++1, ^{81}Br], 635 (52) [M^+, ^{81}Br], 634 (14) [M^++1, ^{79}Br], 633 (51) [M^+, ^{79}Br], 549 (20), 548 (100), 547 (21), 546 (99), 77 (34). HRMS (EI): calcd $C_{19}H_{19}BrF_7N_3O_3$ ([M]$^+$, ^{81}Br) 635.05247, found 635.05228. Anal. Calcd for $C_{26}H_{19}BrF_7N_3O_3$: C, 49.23; H, 3.02; N, 6.62. Found: C, 49.36; H, 2.99; N, 5.89.

3-(6-(2-Bromophenyl)-3-oxo-2-phenyl-4-(trifluoromethyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-1-yl)propanenitrile (15)



Starting from acrylonitrile (63.6 mg, 1.2 mmol) and **2aa** (534 mg, 1 mmol) **15** was isolated by column chromatography as green crystals (317 mg, 65%); mp 76-77 °C.

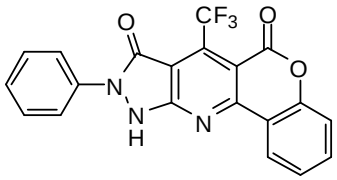
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.57 (t, $^{3}J_{H,H}$ = 6.8 Hz, 2H, $NCH_2\underline{CH_2}$), 4.29 (t, $^{3}J_{H,H}$ = 6.8 Hz, 2H, NCH_2), 7.34-7.41 (m, 2H, Ar), 7.48-7.59 (m, 5H, Ar),

7.66 (dd, $^{3}J_{H,H}$ = 7.7 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 1H, Ar), 7.70 (s, 1H, H-5), 7.76 (dd, $^{3}J_{H,H}$ = 7.7 Hz, $^{4}J_{H,H}$ = 1.4 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.9 ($\underline{C}H_2CN$), 43.9 (NCH_2), 105.7 (C-3a), 116.5 (C≡N), 117.2 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 119.6 (CH_{Ar}), 121.5 (q, $^{1}J_{C,F}$ = 275.1 Hz, CF_3), 121.7 (C_{Ar}), 124.5, 128.1, 129.8, 131.5, 131.6, 134.0 (CH_{Ar}), 136.9 (q, $^{2}J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 138.7, 139.1, 158.1 (C_{Ar}), 160.3 (C=O), 164.0 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.49 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2929 (w), 1693 (m), 1590 (m), 1496 (w), 1410 (w), 1370 (m), 1309 (w), 1281 (m), 1266 (m), 1246 (m), 1181 (w), 1142 (s), 1080 (w), 1055 (w), 1024 (w), 982 (w), 885 (w), 755 (m), 719 (m), 688 (m). MS (EI, 70 eV): *m/z* (%) = 489 (13) [M^++1, ^{81}Br], 488 (57) [M^+, ^{81}Br], 487 (15) [M^++1, ^{79}Br], 486 (56) [M^+, ^{79}Br], 449 (23), 448 (100), 447 (23), 446 (91), 434 (15), 432 (13), 77 (85), 65 (15), 54 (19), 51 (20). HRMS (EI): calcd $C_{22}H_{14}BrF_3N_4O$ ([M]$^+$, ^{81}Br) 488.02791, found 488.02771. Anal. Calcd for $C_{22}H_{14}BrFN_4O$: C, 54.23; H, 2.90; N, 11.50. Found: C, 54.38; H, 2.88; N, 11.46.

A.2.4. General procedure for synthesis of compounds 22

Appropriate 5-amino-1*H*-pyrazol-3(2*H*)-one **4** (1.2 mmol) and corresponding 4-chloro-2*H*-chromen-2-one **21** were placed in a pressure tube and dissolved in absolute DMF (7 mL); chlorotrimethylsilane (600 mg, 5.5 mmol) was added dropwise to the solution. The tube was sealed and heated under an inert atmosphere at 83 ^{o}C for 4-12 h (controlled by TLC). The solution was evaporated under reduced pressure, treated with H_2O, filtered, dried under reduced pressure and recrystallized from an appropriate solvent.

9-Phenyl-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (22a)

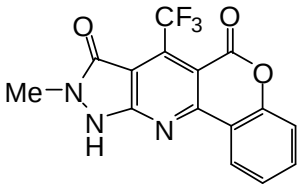


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (210 mg, 1.2 mmol) and 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one **21a** (277 mg, 1 mmol), **22a** was isolated via crystallization from isopropanol as green crystals (258 mg, 65%); mp 296-297 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.33-7.38 (m, 1H, Ar), 7.44-7.51 (m, 2H, Ar), 7.53-7.60 (m, 2H, Ar), 7.71-7.77 (m, 1H, Ar), 7.89-7.92 (m, 2H, Ar), 8.45-8.48 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 96.8 (C-7a), 117.2 (CH_{Ar}), 118.1 (C-6a), 119.9 (CH_{Ar}), 120.9 (q, $^{1}J_{C,F}$ = 274.8 Hz, CF_3), 124.9, 125.0, 125.9, 129.1, 133.8 (CH_{Ar}), 136.3 (C_{Ar}), 138.7 (q, $^{2}J_{C,F}$ = 37.0 Hz, $\underline{C}CF_3$), 142.7 152.6, 155.3 (C_{Ar}), 155.8 (CO-6) 157.9 (CO-8), 158.7 (C-10a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -55.64 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3084 (w), 1749 (m), 1704 (m), 1678 (m), 1583 (s), 1498 (m), 1467 (m), 1410 (m), 1364 (m), 1270 (m), 1234 (m), 1176

(m), 1147 (s), 1075 (w), 1030 (w), 989 (w), 893 (w), 818 (w), 733 (m), 684 (m), 655 (m). MS (EI, 70 eV): *m/z* (%) = 399 (4) [M^++2], 398 (24) [M^++1], 397 (100) [M^+], 377 (45), 368 (18), 77 (33), 73 (15), 60 (14), 44 (21), 43 (12). HRMS (ESI): calcd $C_{20}H_{11}F_3N_3O_3$ ([M+1]$^+$) 398.0747, found 398.07495. Anal. Calcd for $C_{20}H_{10}F_3N_3O_3$: C, 60.46; H, 2.54; N, 10.58. Found: C, 61.01; H, 2.85; N, 9.84.

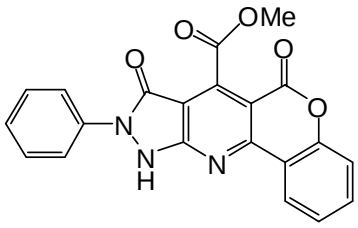
9-Methyl-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (22b)



Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (136 mg, 1.2 mmol) and 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one **21b** (277 mg, 1 mmol), **22b** was isolated via crystallization from isopropanol as yellow crystals (191 mg, 57%); mp >375 ^{o}C.

IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2951 (w), 2719 (w), 2673 (w), 1745 (m), 1645 (m), 1590 (m), 1552 (m), 1464 (m), 1408 (m), 1360 (m), 1285 (w), 1264 (m), 1224 (m), 1202 (m), 1174 (m), 1143 (s), 1108 (m), 1059 (m), 979 (w), 814 (m), 765 (m), 648 (m). MS (EI, 70 eV): *m/z* (%) = 337 (3) [M^++2], 336 (31) [M^++1], 335 (100) [M^+], 315 (33), 287 (66), 264 (10), 43 (8). HRMS (ESI): calcd $C_{15}H_9F_3N_3O_3$ ([M+1]$^+$) 336.05905, found 336.05916. Anal. Calcd for $C_{15}H_8F_3N_3O_3$: C, 53.74; H, 2.41; N, 12.53. Found: C, 54.28; H, 2.36; N, 12.25.

Methyl 6,8-dioxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (22c)

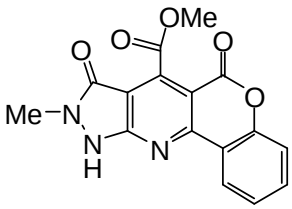


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one **4a** (210 mg, 1.2 mmol) and methyl 2-(4-chloro-2-oxo-2H-chromen-3-yl)-2-oxoacetate **21a** (267 mg, 1 mmol), **22c** was isolated via crystallization from isopropanol as green crystals (232 mg, 60%); mp 295-297 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.97 (s, 3H, OCH_3), 7.28-7.33 (m, 1H, Ar), 7.44-7.49 (m, 2H, Ar), 7.49-7.55 (m, 2H, Ar), 7.68-7.74 (m, 1H, Ar), 7.86-7.89 (m, 2H, Ar), 8.44-8.46 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 53.0 (CH_3), 105.9 (C-7a), 117.2 (CH_{Ar}), 118.0 (C-6a), 120.0, 124.9, 125.1, 125.9, 129.2, 133.8 (CH_{Ar}), 134.7, 136.4, 142.8, 150.7, 152.6 (C_{Ar}), 154.8 (CO-6) 155.9 (CO-8), 158.7 (C-10a), 164.3 ($\underline{C}O_2CH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2928 (w), 2651 (w), 1729 (m), 1688 (w), 1651 (w), 1592 (m), 1580 (m), 1469 (w), 1417 (w), 1366 (m), 1278 (m), 1234 (m), 1142 (w), 1106 (w), 1019 (w), 936 (w), 814 (w), 757 (m), 732 (m), 693 (m), 659 (m). MS (EI, 70 eV): *m/z* (%) = 389 (4) [M^++2], 388 (25) [M^++1], 387 (96) [M^+], 368 (72), 366 (59), 339 (99), 337 (100), 329 (32), 258 (19), 189 (21), 77 (36), 73

(23), 60 (28), 44 (65), 43 (34). HRMS (ESI): calcd $C_{21}H_{14}N_3O_5$ ($[M+1]^+$) 388.0928, found 388.09211. Anal. Calcd for $C_{21}H_{13}N_3O_5$: C, 65.12; H, 3.38; N, 10.85. Found: C, 65.78; H, 3.63; N, 10.004.

Methyl 9-methyl-6,8-dioxo-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (22d)



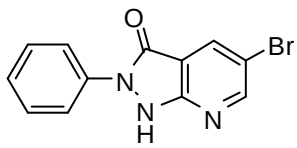
Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one **4b** (136 mg, 1.2 mmol) and methyl 2-(4-chloro-2-oxo-2H-chromen-3-yl)-2-oxoacetate **21b** (267 mg, 1 mmol), **22d** was isolated via crystallization from isopropanol as yellow crystals (221 mg, 68%); mp mp 319-321 ^oC.

^1H NMR (300 MHz, DMSO-d_6): δ = 3.44 (s, 3H, NCH_3), 3.94 (s, 3H, OCH_3), 7.43-7.48 (m, 2H, Ar), 7.67-7.73 (m, 1H, Ar), 8.39-8.42 (m, 1H, Ar), 13.06 (br s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 30.3 (NCH_3), 52.9 (OCH_3), 106.0 (C-7a), 117.1 (CH_{Ar}), 118.4 (C-6a), 124.9, 125.0, 133.5 (CH_{Ar}), 142.2, 152.5, 154.1 (C_{Ar}), 154.5 (CO-6) 155.9 (CO-8), 158.9 (C-10a), 164.4 ($\underline{C}O_2CH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 2725 (w), 1717 (m), 1651 (m), 1604 (m), 1434 (w), 1365 (w), 1278 (m), 1228 (m), 1187 (w), 1137 (w), 1024 (w), 952 (w), 758 (m). MS (EI, 70 eV): *m/z* (%) = 327 (2) [M^++2], 326 (15) [M^++1], 325 (100) [M^+], 294 (13), 267 (40), 196 (10), 43 (2). HRMS (ESI): calcd $C_{16}H_{12}N_3O_5$ ($[M+1]^+$) 326.07715, found 326.07707. Anal. Calcd for $C_{16}H_{11}N_3O_5$: C, 59.08; H, 3.41; N, 12.92. Found: C, 59.34; H, 3.62; N, 12.76.

A.2.5. General procedure for synthesis of compounds 33

Appropriate 5-amino-1*H*-pyrazol-3(2*H*)-one **4** (1 mmol) and 5-bromo-1,2,3-triazine (1.2 mmol) were placed in a flask set with reflux and dissolved in isopropanole (40 mL). The mixture was heated under reflux for 2 h (controlled by TLC). Then the precipitate formed was filtered, washed with hot ethanol, filtered and dried under reduced pressure.

5-Bromo-2-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (33a)

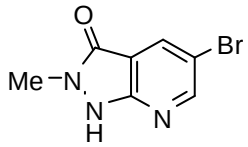


Starting from 5-amino-2-phenyl-1*H*-pyrazol-3(2*H*)-one (175 mg, 1 mmol) **33a** was isolated as brown solid (279 mg, 96%); mp 312-314 ^oC.

MS (EI, 70 eV): *m/z* (%) = 292 (16) [M^++1, ^{81}Br], 291 (100) [M^+, ^{81}Br], 290 (18) [M^++1, ^{79}Br], 289 (99) [M^+, ^{79}Br], 262 (52), 260 (53), 77 (49). HRMS (EI): calcd $C_{12}H_8BrN_3O$ ($[M]^+$,

^{81}Br) 291.11478, found 291.11482. Anal. Calcd for $C_{12}H_8BrN_3O$: C, 49.68; H, 2.78; N, 14.48. Found: C, 49.97; H, 2.91; N, 14.21.

5-Bromo-2-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (33b)

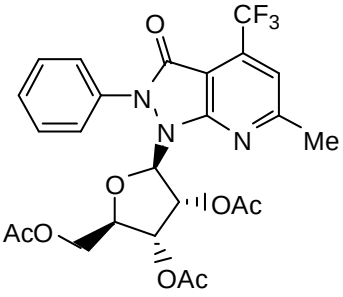


Starting from 5-amino-2-methyl-1*H*-pyrazol-3(2*H*)-one (113 mg, 1 mmol) **36b** was isolated as brown solid (227 mg, quant.); mp >375 ^{o}C. MS (EI, 70 eV): *m/z* (%) = 229 (22) [M^++1, ^{81}Br], 228 (100) [M^+, ^{81}Br], 227 (21) [M^++1, ^{79}Br], 226 (100) [M^+, ^{79}Br], 202 (54), 200 (54), 43 (18). HRMS (EI): calcd $C_7H_6BrN_3O$ ([M]$^+$, ^{81}Br) 228.02447, found 228.02449. Anal. Calcd for $C_7H_6BrN_3O$: C, 36.87; H, 2.65; N, 18.43. Found: C, 37.04; H, 2.71; N, 18.11.

A.2.6. General procedure for synthesis of compounds 37-39

Under argon atmosphere, compound **2, 9, 11, 22** or **33** (1 mmol) was placed in a flask and dry acetonitrile (20 mL) and BSA (0.27 mL, 1.1 mmol) were added. If starting material did not dissolve by refluxing, another portion of BSA (0.27 mL, 1.1 mmol) was added. After refluxing for 20 minutes the solution was led to cool down to room temperature. Afterwards, the solution of corresponding acetylated sugar (1 mmol) in dry acetonitrile and TMSOTf (0.05 mL, 0.25 mmol) were added and the reaction mixture was refluxed for 2 hours (controlled by TLC). Then the solution was evaporated under reduced pressure and subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

6-Methyl-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37a)

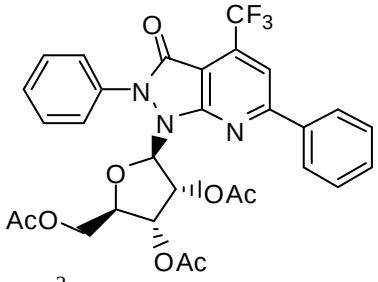


Starting from **2a** (293 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37a** was isolated as colorless foam (452 mg, 82%); mp 84-86 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3H, OAc-5'), 2.07 (s, 3H, OAc-3'), 2.11 (s, 3H, OAc-2'), 2.80 (s, 3H, CCH_3), 3.80-3.87 (m, 1H, H_a-5'), 4.07-4.14 (m, 2H, H_b-5', H-4'), 5.52 (t, $^3J_{H,H}$ = 5.9 Hz, 1H, H-3'), 5.63 (d, $^3J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.35 (dd, $^3J_{H,H}$ = 5.9 Hz, $^3J_{H,H}$ = 4.3 Hz, 1H, H-2'), 7.32-7.37 (m, 1H, Ph), 7.37 (s, 1H, H-5), 7.46-7.51 (m, 2H, Ph), 7.56-7.56 (m, 2H, Ph).^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.6, 20.6, 20.7 ($\underline{C}H_3CO$), 25.4 (CH_3), 62.8 (CH_2), 69.6, 72.2, 78.4, 92.0 (CH_{rib}), 106.2 (C-3a), 116.2 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.4 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 124.5, 127.4, 129.2 (CH_{Ar}), 135.0 (C_{Ar}), 136.5 (q, $^2J_{C,F}$ = 36.6 Hz,

$\underline{C}CF_3$), 158.5 (C_{Ar}), 160.3 (CO), 165.3 (C-7a), 169.3, 169.4, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.72 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 2943 (w), 1745 (m), 1708 (m), 1592 (m), 1487 (w), 1430 (w), 1363 (m), 1229 (s), 1145 (s), 1043 (m), 897 (w), 753 (w), 698 (w). MS (EI, 70 eV): *m/z* (%) = 551 (0.13) [M^+], 293 (17), 259 (88), 139 (100), 97 (45), 77 (21), 43 (55). HRMS (ESI): calcd $C_{25}H_{25}F_3N_3O_8$ ([M+1]$^+$) 552.1588, found 552.1581. Anal. Calcd for $C_{25}H_{24}F_3N_3O_8$: C, 54.45; H, 4.39; N, 7.62 Found: C, 54.53; H, 4.29; N, 7.60.

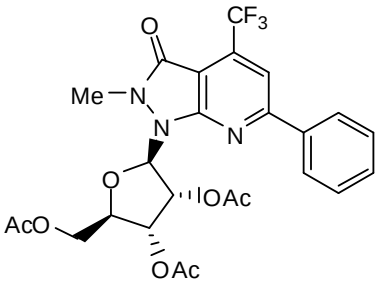
2,6-Biphenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37b)



Starting from **2c** (355 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **40b** was isolated as yellow foam (491 mg, 80%); mp 138-139 ^oC.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.69 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.81 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 5.2 Hz, 1H, H_a-5'), 4.01 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 3.4 Hz, 1H, H_b-5'), 4.06-4.11 (m, 1H, H-4'), 5.41 (t, $^3J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.65 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.58 (dd, $^3J_{H,H}$ = 6.4 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, H-2'), 7.35 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ph), 7.50 (t, $^3J_{H,H}$ = 7.4 Hz, 2H, Ph), 7.55-7.63 (m, 5H, Ph), 7.97 (s, 1H, H-5), 8.24-8.25 (m, 2H, Ph). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.5 ($\underline{C}H_3CO$), 62.2 (CH_2), 69.2, 72.0, 78.4, 92.4 (CH_{rib}), 107.1 (C-3a), 113.0 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^1J_{C,F}$ = 274.0 Hz, CF_3), 124.6, 127.5, 128.0, 129.3, 129.5, 131.6 (CH_{Ar}), 135.0, 136.4 (C_{Ar}), 137.3 (q, $^2J_{C,F}$ = 36.7 Hz, $\underline{C}CF_3$), 158.4 (C_{Ar}), 160.6 (C=O), 162.3 (C-7a), 169.4, 169.4, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.65 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3009 (w), 2947 (w), 1738 (m), 1699 (m), 1593 (m), 1489 (w), 1372 (s), 1234 (s), 1216(s), 1147 (s), 1104 (m), 1033 (s), 903 (m), 879 (m), 760 (m), 728 (m), 693 (s), 585 (m). MS (EI, 70 eV): *m/z* (%) = 614 (0.38) [M^++1], 613 (0.15) [M^+], 355 (41), 259 (99), 157 (23), 139 (100), 97 (75), 77 (43), 43 (97). HRMS (ESI): calcd $C_{30}H_{27}F_3N_3O_8$ ([M+1]$^+$) 614.1745, found 614.1747. Anal. Calcd for $C_{30}H_{26}F_3N_3O_8$: C, 58.73; H, 4.27; N, 6.85. Found: C, 58.64; H, 4.41; N, 6.71.

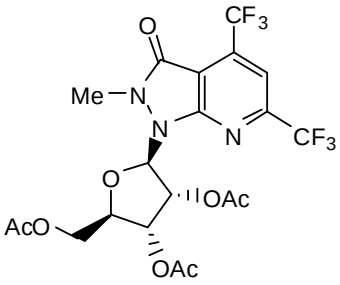
2-Methyl-6-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37c)



Starting from **2d** (293 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37c** was isolated as yellow foam (381 mg, 69%); mp 76-78 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.69 (s, 3H, OAc-5'), 2.01 (s, 3H, OAc-3'), 2.05 (s, 3H, OAc-2'), 3.48 (s, 3H, NCH_3), 3.94 (dd, $^{2}J_{H,H}$ = 12.2 Hz, $^{3}J_{H,H}$ = 4.8 Hz, 1H, H-5'$_a$), 4.10 (dd, $^{2}J_{H,H}$ = 12.2 Hz, $^{2}J_{H,H}$ = 3.0 Hz, 1H, H-5'$_b$), 4.13-4.19 (m, 1H, H-4'), 5.46 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.81 (d, $^{3}J_{H,H}$ = 4.5 Hz, 1H, H-1'), 6.32 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.5 Hz, 1H, H-2'), 7.46-7.50 m, (3H, Ph), 7.80 (s, 1H, H-5), 8.07-8.11 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.4, 20.4 ($CO\underline{C}H_3$), 31.2 (CH_3), 62.2 (CH_2), 69.2, 71.6, 78.5, 90.7 (CH_{rib}), 106.4 (C-3a), 112.2 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^{1}J_{C,F}$ = 274.7 Hz, CF_3), 127.8, 129.3, 131.3 (CH_{Ar}), 136.5 (C_{Ar}), 136.6 (q, $^{2}J_{C,F}$ = 36.4 Hz, $\underline{C}CF_3$), 159.0 (C_{Ar}), 159.4 (C=O), 161.6 (C-7a), 169.4, 169.3, 170.3 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.61 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2945 (w), 1743 (m), 1693 (m), 1595 (m), 1372 (m), 1218 (s), 1146 (m), 1039 (m), 776 (m), 692 (m). HRMS (ESI): calcd $C_{25}H_{25}F_3N_3O_8$ ($[M+1]^+$) 552.1588, found 552.1582. Anal. Calcd for $C_{25}H_{24}F_3N_3O_8$: C, 54.45; H, 4.39; N, 7.62. Found: C, 54.58; H, 4.31; N, 7.54.

2-Methyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37d)

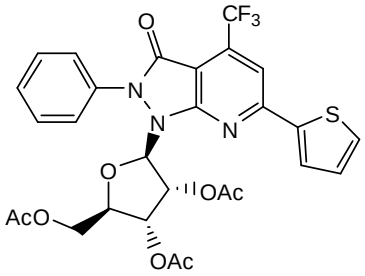


Starting from **2f** (285 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37d** was isolated as yellow solid (500 mg, 92%); mp 103-105 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.92 (s, 3H, OAc-5'), 1.97 (s, 3H, OAc-3'), 2.07 (s, 3H, OAc-2'), 3.53 (s, 3H, NCH_3), 4.06 (dd, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 6.0 Hz, 1H, H-5'$_a$), 4.18-4.21 (m, 1H, H-5'$_b$), 4.22-4.24 (m, 1H, H-4'), 5.40 (t, $^{3}J_{H,H}$ = 6.2 Hz, 1H, H-3'), 5.87 (d, $^{3}J_{H,H}$ = 4.7 Hz, 1H, H-1'), 6.51 (dd, $^{3}J_{H,H}$ = 6.2 Hz, $^{3}J_{H,H}$ = 4.7 Hz, 1H, H-2'), 7.61 (s, 1H, H-5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.2, 20.4, 20.5 ($CO\underline{C}H_3$), 31.6 (CH_3), 62.3 (CH_2), 69.2, 71.1, 78.8, 90.9 (CH_{sug}), 110.6 (C-3a), 111.5 (q, $^{3}J_{C,F}$ = 2.6 Hz, C-5), 120.3 (q, $^{1}J_{C,F}$ = 275.3 Hz, CF_3), 120.8 (q, $^{1}J_{C,F}$ = 275.3 Hz, CF_3), 138.4 (q, $^{2}J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 151.2 (q, $^{2}J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 157.4 (C=O), 157.7 (C-7a), 169.2, 169.3, 170.2 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -67.80 (s), -62.43 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2150 (w), 2837 (br), 1745 (s), 1703 (s),

1606 (w), 1375 (m), 1273 (s), 1209 (s), 1145 (s), 1042 (s), 883 (m), 686 (m), 602 (m). HRMS (ESI): calcd $C_{20}H_{19}F_6N_3NaO_8$ ($[M+1]^+$) 566.0969, found 566.098. Anal. Calcd for $C_{20}H_{19}F_6N_3O_8$: C, 44.21; H, 3.52; N, 7.73. Found: C, 44.37; H, 3.49; N, 7.59.

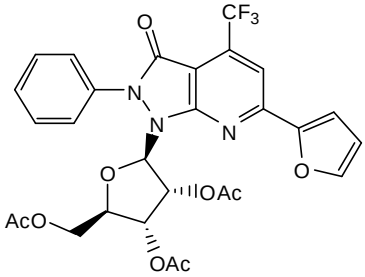
2-Phenyl-6-(thiophen-2-yl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37e)



Starting from **2g** (361 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37e** was isolated as yellow foam (582 mg, 94%); mp 88-90 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (s, 3H, OAc-5'), 2.09 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.89 (dd, $^2J_{H,H}$ = 13.0 Hz, $^3J_{H,H}$ = 6.4 Hz, 1H, H_a-5'), 4.05-4.12 (m, 2H, H_b-5', H-4'), 5.47 (t, $^3J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.58 (d, $^3J_{H,H}$ = 4.5 Hz, 1H, H-1'), 6.58 (dd, $^3J_{H,H}$ = 6.4 Hz, $^3J_{H,H}$ = 4.5 Hz, 1H, H-2'), 7.22 (dd, $^2J_{H,H}$ = 5.1 Hz, $^3J_{H,H}$ = 3.8 Hz, 1H, Ar), 7.32-7.38 (m, 1H, Ar), 7.47-7.52 (m, 2H, Ar), 7.58-7.63 (m, 3H, Ar), 7.79 (s, 1H, H-5), 7.93 (dd, $^3J_{H,H}$ = 3.8 Hz, $^3J_{H,H}$ = 1.1 Hz, 1H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4, 20.6 ($\underline{C}H_3CO$), 62.6 (CH_2), 69.6, 71.9, 78.9, 92.5 (CH_{rib}), 106.7 (C-3a), 111.9 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.5 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 124.5, 127.5, 129.1, 129.2, 129.4, 131.8 (CH_{Ar}), 135.1 (C_{Ar}), 137.4 (q, $^2J_{C,F}$ = 36.9 Hz, $\underline{C}CF_3$), 142.3, 157.1 (C_{Ar}), 158.4 (CO), 160.6 (C-7a), 168.9, 169.4, 169.5, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.87 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3100 (w), 2944 (w), 1745 (m), 1705 (m), 1589 (m), 1537 (w), 1488 (w), 1424 (m), 1374 (m), 1221 (s), 1144 (s), 1060 (m), 1039 (m), 899 (w), 715 (m). MS (EI, 70 eV): *m/z* (%) = 620 (0.30) [M^+], 362 (16), 361 (53), 360 (14), 260 (25), 259 (100), 157 (27), 139 (100), 97 (90), 77 (44), 43 (99). HRMS (ESI): calcd $C_{28}H_{25}F_3N_3O_8S$ ($[M+1]^+$) 620.1309, found 620.13015. Anal. Calcd for $C_{28}H_{24}F_3N_3O_8S$: C, 54.28; H, 3.90; N, 6.78. Found: C, 54.42; H, 4.12; N, 6.68.

2-Phenyl-6-(furan-2-yl)-1-(2,3,5-Tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37f)

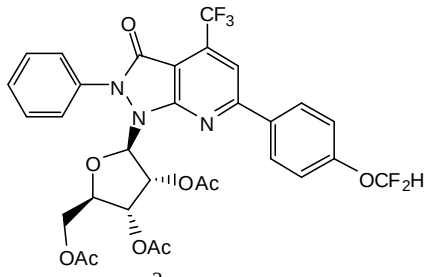


Starting from **2i** (345 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37f** was isolated as colorless foam (500 mg, 83%); mp 142-143 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72 (s, 3H, OAc-5'), 2.10 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.83-3.89 (m, 1H, H-5'$_a$), 4.06-4.13 (m, 2H, H-5'$_b$, H-4'), 5.51 (d, $^3J_{H,H}$ = 3.3 Hz, 1H, H-

3'), 5.58 (dd, $^{3}J_{H,H}$ = 7.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H, H-1'), 6.59 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-2'), 6.68 (dd, $^{3}J_{H,H}$ = 3.3 Hz, $^{3}J_{H,H}$ = 2.0 Hz, 1H, H-4'), 7.31-7.37 (m, 1H, Ar/Hetar), 7.47-7.52 (m, 2H, Ar/Hetar), 7.52-7.55 (m, 2H, Ar/Hetar), 7.67-7.68 (m, 2H, Ar/Hetar), 7.91 (s, 1H, H-5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.2, 20.4, 20.5 ($\underline{C}H_3CO$), 62.0 (CH_2), 68.9, 72.4, 78.1, 92.5 (CH_{rib}), 106.6 (C-3a), 111.3 (q, $^{3}J_{C,F}$ = 5.5 Hz, C-5), 113.5, 114.4 ($CH_{Ar/Hetar}$), 121.3 (q, $^{1}J_{C,F}$ = 274.0 Hz, CF_3), 124.4, 127.3, 129.2, ($CH_{Ar/Hetar}$), 134.7 ($C_{Ar/Hetar}$), 137.3 (q, $^{2}J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 145.9 ($CH_{Ar/Hetar}$), 151.6, 153.0 ($C_{Ar/Hetar}$), 158.1 (C=O), 160.3 (C-7a), 169.4, 169.6, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.85 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3098 (w), 2889 (w), 1751 (m), 1700 (m), 1569 (m), 1527 (w), 1497 (w), 1431 (m), 1368 (m), 1221 (s), 1140 (s), 1059 (m), 1034 (m), 901 (w), 715 (m). MS (EI, 70 eV): *m/z* (%) = 604 (0.8) [M^++1], 345 (98), 316 (44), 259 (100), 157 (80), 139 (100), 97 (98), 85 (29), 77 (95), 69 (50), 43 (100). HRMS (ESI): calcd $C_{28}H_{25}F_3N_3O_9$ ([M+1]$^+$) 604.15374, found 604.15529. Anal. Calcd for $C_{28}H_{24}F_3N_3O_9$: C, 55.72; H, 4.01; N, 6.96. Found: C, 55.49; H, 3.95; N, 6.57.

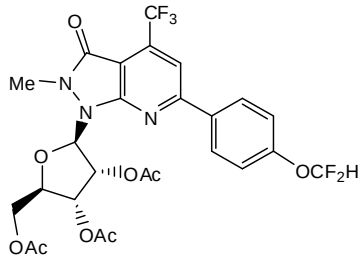
6-(4-(Difluoromethoxy)phenyl)-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37g)



Starting from **2r** (421 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **40g** was isolated as yellow foam (571 mg, 84%); mp 150-152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.72 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.13 (s, 3H, OAc-2'), 3.79 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 5.2 Hz, 1H, H_a-5'), 4.02 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H_b-5'), 4.06-4.12 (m, 1H, H-4'), 5.39 (t, $^{3}J_{H,H}$ = 6.5 Hz, 1H, H-3'), 5.62 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.60 (dd, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-2'), 6.64 (t, $^{2}J_{F,H}$ = 73.3 Hz, 1H, OCF_2H), 7.30-7.33 (m, 2H, Ar), 7.36-7.39 (m, 1H, Ar), 7.48-7.53 (m, 2H, Ar), 7.59-7.63 (m, 2H, Ar), 7.93 (s, 1H, H-5), 8.26-8.31 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4, 20.5, 20.6 ($\underline{C}H_3CO$), 62.3 (CH_2), 96.3, 72.0, 78.3, 92.5 (CH_{rib}), 107.3 (C-3a), 112.7 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 115.6 (t, $^{1}J_{C,F}$ = 260.9 Hz, OCF_2H), 117.7 (q, $^{1}J_{C,F}$ = 254.8 Hz, CF_3), 119.9, 124.7, 127.6, 129.4, 129.9 (CH_{Ar}), 133.4, 134.9 (C_{Ar}), 137.6 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 153.9 (t, $^{3}J_{C,F}$ = 2.8 Hz, $\underline{C}OCF_2H$), 158.3 (C_{Ar}), 160.6 (C=O), 161.0 (C-7a), 169.5, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -81.53 (s, 2F, OCF_2H), -62.68 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 1742 (m), 1690 (m), 1593 (m), 1497 (w), 1371 (s), 1226 (s), 1113 (s), 1022 (s), 910 (m), 887 (m), 846 (m), 751 (m), 698 (m). MS (EI, 70 eV): *m/z* (%) = 680 (0.09) [M^+], 421 (13), 259 (89), 157 (13), 139 (100), 97 (47), 77 (29), 43 (92). HRMS (ESI): calcd $C_{31}H_{27}F_5N_3O_9$

([M+1]$^+$) 680.1662, found 680.1662. Anal. Calcd for $C_{31}H_{26}F_5N_3O_9$: C, 54.79; H, 3.86; N, 6.18 Found: C, 54.42; H, 3.62; N, 5,92.

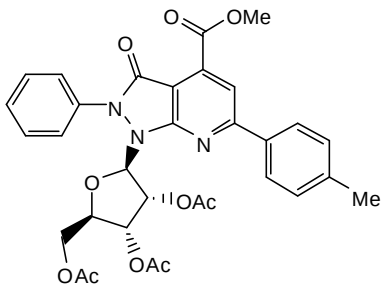
6-(4-(Difluoromethoxy)phenyl)-2-methyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37h)



Starting from **2s** (359 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37h** was isolated as yellow foam (364 mg, 59%); mp 116-118 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (s, 3H, OAc-5'), 2.10 (s, 3H, OAc-3'), 2.13 (s, 3H, OAc-2'), 3.55 (s, 3H, NCH_3), 3.98 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 4.9 Hz, 1H, H-5'$_a$), 4.17 (dd, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,H}$ = 3.3 Hz, 1H, H-5'$_b$), 4.21-4.26 (1H, br m, H-4'), 5.51 (t, $^3J_{H,H}$ = 6.3 Hz, 1H, H-3'), 5.84 (d, $^3J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.44 (dd, $^3J_{H,H}$ = 6.3 Hz, $^3J_{H,H}$ = 4.3 Hz, 1H, H-2'), 6.63 (t, $^2J_{H,F}$ = 73.3 Hz, 1H, OCF_2H), 7.28-7.31 (m, 2H, Ar), 7.83 (s, 1H, H-5), 8.18-8.23 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.5 ($CO\underline{C}H_3$), 31.0 (CH_3), 62.3 (CH_2), 69.2, 71.7, 78.4, 90.7 (CH_{rib}), 106.6 (C-3a), 111.9 (q, $^3J_{C,F}$ = 5.1 Hz, C-5), 115.5 (t, $^1J_{C,F}$ = 261.1 Hz, OCF_2H), 119.8 (CH_{Ar}), 121.5 (q, $^1J_{C,F}$ = 275.0 Hz, CF_3), 129.6 (CH_{Ar}), 133.5 (C_{Ar}), 136.9 (q, $^2J_{C,F}$ = 36.5 Hz, $\underline{C}CF_3$), 153.6 (t, $^3J_{C,F}$ = 2.8 Hz, $\underline{C}OCF_2H$), 159.0 (C_{Ar}), 159.1 (C=O), 160.3 (C-7a), 169.4, 169.4, 170.2 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -81.49 (s, 2F, OCF_2H), -62.64 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2949 (w), 1746 (m), 1700 (s), 1590 (m), 1498 (w), 1368 (s), 1201 (s), 1105 (s), 1014 (s), 908 (m), 873 (m), 760 (m), 668 (m). MS (EI, 70 eV): *m/z* (%) = 618 (0.4) [M$^+$+1], 617 (0.2) [M$^+$], 359 (95), 331 (23), 259 (100), 157 (71), 139 (100), 97 (99), 85 (23), 69 (39), 43 (100). HRMS (ESI): calcd $C_{26}H_{25}F_5N_3O_9$ ([M+1]$^+$) 618.15055, found 618.15131. Anal. Calcd for $C_{26}H_{24}F_5N_3O_9$: C, 50.57; H, 3.92; N, 6.81. Found: C, 50.34; H, 4.05; N, 7.08.

Methyl 3-oxo-2-phenyl-6-*p*-tolyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (37i)

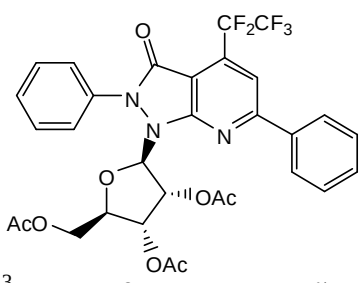


Starting from **2u** (359 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37i** was isolated as yellow foam (537 mg, 87%); mp 100-101 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.11 (s, 3H, OAc-2'), 2.45 (s, 3H, Ar-CH_3), 3.77 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 5.1 Hz, 1H, H-5'$_a$), 4.00 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 3.4 Hz, 1H, H-5'$_b$), 4.05 (s, 3H, OCH_3), 4.06-4.08 (br m, 1H, H-4'),

5.42 (t, $^{3}J_{H,H}$ = 6.5 Hz, 1H, H-3'), 5.61 (d, $^{3}J_{H,H}$ = 3.9 Hz, 1H, H-1'), 6.58 (dd, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 3.9 Hz, 1H, H-2'), 7.31-7.37 (m, 3H, Ar), 7.46-7.51 (m, 2H, Ar), 7.60-7.63 (m, 2H, Ar), 8.01 (s, 1H, H-5), 8.14-8.16 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.4, 20.5 ($\underline{C}H_3CO$), 21.4 (CH_3), 53.2 (OCH_3), 62.2 (CH_2), 69.2, 72.0, 78.2, 92.5 (CH_{rib}), 107.8 (C-3a), 115.9, 124.5, 127.2, 127.8, 129.1, 130.0 (CH_{Ar}), 133.8, 135.3, 139.4, 141.7, 159.4 (C_{Ar}), 160.4 (C=O), 161.5 (C-7a), 165.3 ($\underline{C}O_2CH_3$), 169.3, 169.3, 170.3 ($CH_3\underline{C}O$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2949 (w), 1743 (m), 1704 (m), 1583 (m), 1362 (m), 1213 (s), 1043 (m), 1018 (m), 896 (w), 824 (w), 736 (m). MS (EI, 70 eV): *m/z* (%) = 617 (0.79) [M^+], 359 (100), 301 (15), 299 (22), 259 (83), 139 (83), 97 (28), 77 (12), 71 (12), 43 (87). HRMS (ESI): calcd $C_{32}H_{32}N_3O_{10}$ ([M+1]$^+$) 618.2082, found 618.2077. Anal. Calcd for $C_{32}H_{31}N_3O_{10}$: C, 62.23; H, 5.06; N, 6.80 Found: C, 62.16; H, 5.05; N, 6.45.

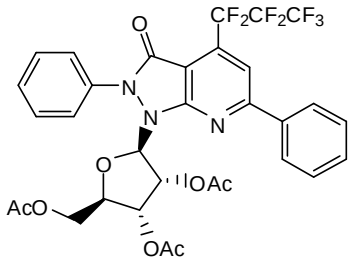
2,6-Biphenyl-4-(perfluoroethyl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37j)



Starting from **2v** (405 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37j** was isolated as yellow foam (544 mg, 82%); mp 156-158 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.69 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.81 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 5.0 Hz, 1H, H_a-5'), 4.02 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H_b-5'), 4.05-4.11 (m, 1H, H-4'), 5.40 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.65 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.60 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-2'), 7.33-7.39 (m, 1H, Ph), 7.47-7.53 (m, 2H, Ph), 7.57-7.65 (m, 5H, Ph), 7.93 (s, 1H, H-5), 8.22-8.26 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.6, 20.6 ($\underline{C}H_3CO$), 62.3 (CH_2), 69.3, 72.1, 78.4, 92.6 (CH_{rib}), 108.3 (C-3a), 115.0 (t, $^{3}J_{C,F}$ = 7.8 Hz, C-5), 124.8, 127.5, 128.0, 129.3, 129.5, 131.6 (CH_{Ar}), 135.0, 136.4 (C_{Ar}), 137.3 (q, $^{2}J_{C,F}$ = 36.7 Hz, $\underline{C}CF_2$), 158.4 (C_{Ar}), 160.6 (C=O), 162.3 (C-7a), 169.4, 169.4, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -111.7 0 (s, 2F, CF_2), -83.17 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2924 (w), 2853 (w), 1746 (m), 1710 (m), 1588 (m), 1579 (w), 1495 (w), 1444 (w), 1366 (m), 1327 (m), 1201 (s), 1150 (m), 1089 (w), 1049 (m), 1015 (m), 901 (w), 865 (w), 774 (m), 733 (m), 691 (m). MS (EI, 70 eV): *m/z* (%) = 664 (0.72) [M^++1], 663 (0.52) [M^+], 406 (40), 405 (71), 404 (27), 376 (19), 260 (61), 259 (93), 157 (68), 140 (40), 139 (100), 97 (83), 77 (64), 69 (21), 43 (87). HRMS (ESI): calcd $C_{31}H_{27}F_5N_3O_8$ ([M+1]$^+$) 664.1713, found 664.1709. Anal. Calcd for $C_{31}H_{26}F_5N_3O_8$: C, 56.11; H, 3.95; N, 6.33. Found: C, 56.26; H, 3.97; N, 6.51.

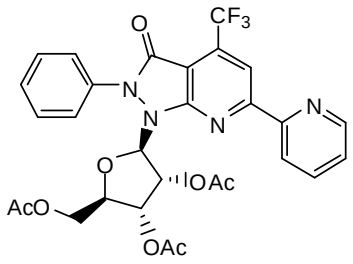
2,6-Biphenyl-4-(perfluoropropyl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37k)



Starting from **2w** (455 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37k** was isolated as yellow foam (542 mg, 76%); mp 121-123 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.81-3.85 (m, 1H, H_a-5'), 4.02 (dd, $^{2}J_{H,H}$ = 12.2 Hz, $^{3}J_{H,H}$ = 3.5 Hz, 1H, H_b-5'), 4.08-4.12 (m, 1H, H-4'), 5.41 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.65 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.60 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-2'), 7.33-7.39 (m, 1H, Ph), 7.47-7.53 (m, 2H, Ph), 7.57-7.65 (m, 5H, Ph), 7.93 (s, 1H, H-5), 8.22-8.26 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.6, 20.6 ($\underline{C}H_3CO$), 62.3 (CH_2), 69.3, 72.1, 78.4, 92.6 (CH_{rib}), 108.3 (C-3a), 115.0 (t, $^{3}J_{C,F}$ = 7.8 Hz, C-5), 124.8 (CH_{Ar}), 127.5, 128.0, 129.3, 129.5, 131.6 (CH_{Ar}), 135.0, 136.4 (C_{Ar}), 137.3 (t, $^{2}J_{C,F}$ = 36.0 Hz, $\underline{C}CF_2$), 158.4 (C_{Ar}), 160.6 (C=O), 162.3 (C-7a), 169.4, 169.4, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -79.96 (t, $^{3}J_{F,F}$ = 9.7 Hz, 3F, CF_3), -112.74 (dq, $^{2}J_{F,F}$ = 275.0 Hz, $^{3}J_{F,F}$ = 9.7 Hz, 1F, CF_3), -115.27 (dq, $^{2}J_{F,F}$ = 275.0 Hz, $^{3}J_{F,F}$ = 9.7 Hz, 1F, CF_3), -125.54 (s, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 714 (0.2) [M^++1], 713 (0.1) [M^+], 455 (23), 454 (19), 260 (11), 259 (100), 157 (14), 139 (96), 97 (39), 77 (23), 43 (52). HRMS (ESI): calcd $C_{32}H_{27}F_7N_3O_8$ ([M+1]$^+$) 714.16809, found 714.1689. Anal. Calcd for $C_{32}H_{26}F_7N_3O_8$: C, 53.86; H, 3.67; N, 5.89. Found: C, 53.95; H, 3.69; N, 5.87.

2-Phenyl-6-(pyridin-2-yl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-4-(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (37l)

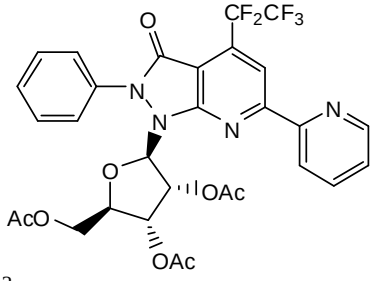


Starting from **2x** (356 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37l** was isolated as yellow foam (504 mg, 82%); mp 66-67 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.93 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.08 (s, 3H, OAc-2'), 3.81 (dd, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H_a-5'), 4.06-4.13 (m, 2H, H_b-5', H-4'), 5.33 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.70 (d, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.25 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-2'), 7.36-7.45 (m, 2H, Ar), 7.48-7.54 (m, 2H, Ar), 7.60-7.63 (m, 2H, Ar), 7.85 (td, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, Ar), 8.33 (s, 1H, H-5), 8.57 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.79-8.82 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.7 ($\underline{C}H_3CO$), 62.7 (CH_2), 69.5, 72.0, 78.8, 92.8 (CH_{rib}), 111.6 (C-3a), 117.1 (q, $^{3}J_{C,F}$ = 2.8 Hz, C-5), 121.2 (q, $^{1}J_{C,F}$ = 275.6 Hz, CF_3), 125.1, 125.2, 127.5, 128.0, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 136.6, 150.1 (CH_{Ar}), 150.4 (C_{Ar}), 151.0 (q,

$^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 151.3 (C_{Ar}), 159.6 (C=O), 160.0 (C-7a), 169.3, 169.4, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -67.62 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3063 (w), 2947 (w), 1747 (m), 1698 (w), 1588 (w), 1567 (w), 1470 (w), 1372 (w), 1269 (m), 1224 (s), 1182 (m), 1142 (m), 1094 (m), 1038 (m), 885 (w), 787 (w), 751 (w), 730 (w). MS (EI, 70 eV): *m/z* (%) = 614 (0.14) [M^+], 356 (16), 355 (14), 259 (55), 157 (10), 139 (77), 97 (41), 77 (17), 43 (100). HRMS (ESI): calcd $C_{29}H_{26}F_3N_4O_8$ ([M+1]$^+$) 615.1697, found 615.17. Anal. Calcd for $C_{29}H_{25}F_3N_4O_8$: C, 56.68; H, 4.10; N, 9.12. Found: C, 56.87; H, 4.15; N, 9.09.

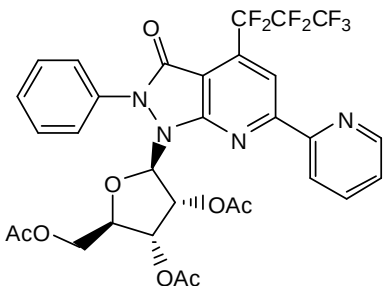
4-(Perfluoroethyl)-2-phenyl-6-(pyridin-2-yl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (37m)



Starting from **2y** (406 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37m** was isolated as yellow foam (545 mg, 82%); mp 65-66 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (s, 3H, OAc-5'), 2.06 (s, 3H, OAc-3'), 2.07 (s, 3H, OAc-2'), 3.80 (dd, $^{2}J_{H,H}$ = 13.1 Hz, $^{3}J_{H,H}$ = 7.1 Hz, 1H, H_a-5'), 4.08-4.15 (m, 2H, H_b-5', H-4'), 5.45 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.68 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.28 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-2'), 7.36-7.44 (m, 2H, Ar), 7.49-7.54 (m, 2H, Ar), 7.59-7.62 (m, 2H, Ar), 7.35 (td, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.9 Hz, 1H, Ar), 8.31 (s, 1H, H-5), 8.57 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.79-8.81 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.5, 20.7 ($\underline{C}H_3CO$), 62.8 (CH_2), 69.5, 71.7, 78.7, 92.8 (CH_{rib}), 111.5 (C-3a), 118.5 (C-5), 125.2, 125.3, 127.6, 128.1, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 136.6 (CH_{Ar}), 139.2 (t, $^{2}J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 150.1 (CH_{Ar}), 150.4, 151.1 (C_{Ar}), 159.4 (C=O), 160.0 (C-7a), 169.3, 169.3, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -82.51 (s, 3F, CF_3), -116.48 (dd, $^{2}J_{F,F}$ = 667.57 Hz, $^{3}J_{F,F}$ = 273.39 Hz, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2929 (w), 1746 (m), 1704 (m), 1588 (w), 1567 (w), 1495 (w), 1469 (w), 1372 (m), 1331 (w), 1205 (s), 1095 (m), 1040 (m), 1013 (s), 874 (m), 787 (w), 743 (m), 693 (m). MS (EI, 70 eV): *m/z* (%) = 664 (0.1) [M^+], 532 (27), 531 (29), 439 (57), 259 (58), 157 (14), 139 (100), 97 (42), 84 (33), 77 (16), 57 (47), 43 (88). HRMS (ESI): calcd $C_{30}H_{26}F_5N_4O_8$ ([M+1]$^+$) 665.1665, found 665.1668. Anal. Calcd for $C_{30}H_{25}F_5N_4O_8$: C, 54.22; H, 3.79; N, 8.43. Found: C, 54.34; H, 3.80; N, 8.39.

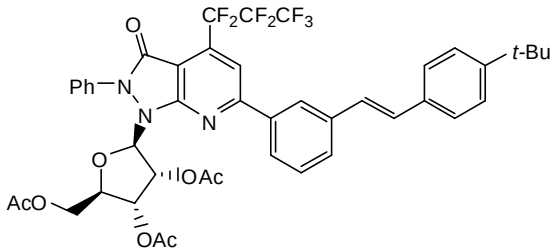
4-(Perfluoropropyl)-2-phenyl-6-(pyridin-2-yl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (37n)



Starting from **2z** (456 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37n** was isolated as yellow foam (607 mg, 85%); mp 84-85 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3H, OAc-5'), 2.05 (s, 3H, OAc-3'), 2.06 (s, 3H, OAc-2'), 3.77-3.83 (m, 1H, H_a-5'), 4.05-4.12 (m, 2H, H_b-5', H-4'), 5.31 (t, $^{3}J_{H,H}$ = 6.3 Hz, 1H, H-3'), 5.73 (d, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.20 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-2'), 7.36-7.46 (m, 2H, Ar), 7.49-7.54 (m, 2H, Ar), 7.48-7.54 (m, 2H, Ar), 7.59-7.63 (m, 2H, Ar), 7.87 (td, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, Ar), 8.32 (s, 1H, H-5), 8.58 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.0 Hz, 1H, Ar), 8.79-8.82 (m, 1H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4, 20.5, 20.7 ($\underline{C}H_3CO$), 62.8 (CH_2), 69.5, 71.6, 78.7, 92.8 (CH_{rib}), 111.4 (C-3a), 118.8 (t, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 124.8, 125.4, 127.8, 128.2, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 137.1, 149.6 (CH_{Ar}), 139.2 (t, $^{2}J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 150.5, 150.8 (C_{Ar}), 159.4 (C=O), 160.0 (C-7a), 169.3, 169.3, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -80.12 (t, $^{3}J_{F,F}$ = 9.6 Hz, 3F, CF_3), -113.04 (dq, $^{2}J_{F,F}$ = 274.6 Hz, $^{3}J_{F,F}$ = 9.6 Hz, 1F, CF_3), -115.41 (dq, $^{2}J_{F,F}$ = 274.6 Hz, $^{3}J_{F,F}$ = 9.6 Hz, 1F, CF_3), -125.84 (s, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 715 (0.2) [M+1], 714 (0.16) [M^+], 456 (25), 260 (12), 259 (93), 157 (20), 139 (100), 97 (54), 77 (13), 43 (77). HRMS (ESI): calcd $C_{31}H_{26}F_7N_4O_8$ ([M+1]$^+$) 715.16334, found 715.16375. Anal. Calcd for $C_{31}H_{25}F_7N_4O_8$: C, 52.11; H, 3.53; N, 7.84. Found: C, 51.895; H, 3.515; N, 7.866.

(*E*)-6-(3-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37o)

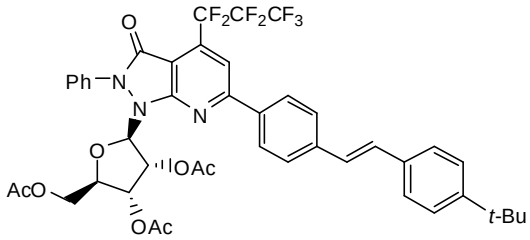


Starting from **9a** (614 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37o** was isolated as yellow foam (610 mg, 70%); mp 95-96 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9H, CH_3), 1.70 (s, 3H, OAc-5'), 2.06 (s, 3H, OAc-3'), 2.14 (s, 3H, OAc-2'), 3.82 (dd, $^{2}J_{H,H}$ = 12.3 Hz, $^{3}J_{H,H}$ = 5.1 Hz, 1H, H_a-5'), 4.02 (dd, $^{2}J_{H,H}$ = 12.3 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H_b-5'), 4.07-4.13 (m, 1H, H-4'), 5.41 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.66 (d, $^{3}J_{H,H}$ = 4.1 Hz, 1H, H-1'), 6.70 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.1 Hz, 1H, H-2'), 7.28-7.30 (m, 1H, Ar), 7.34-7.43 (m, 3H, Ar, =CH), 7.49-7.66 (m, 8H, Ph, =CH), 7.77 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.95 (s, 1H, H-5), 8.08 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.33 (s, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.6

($\underline{C}H_3CO$), 31.4 (CH_3), 34.7 ($\underline{C}(CH_3)_3$), 62.3 (CH_2), 69.5, 72.0, 78.5, 92.6 (CH_{rib}), 108.7 (C-3a), 115.3 (t, $^3J_{C,F}$ = 8.5 Hz, C-5), 124.9, 125.8, 126.5, 126.6, 126.9, 127.3, 127.6, 128.8, 129.4, 129.8, 129.9 (CH_{Ar}, =CH), 134.5, 135.1, 136.8 (C_{Ar}), 137.0 (t, $^2J_{C,F}$ = 26.3 Hz, $\underline{C}CF_2$), 139.1, 151.3, 158.0 (C_{Ar}), 160.5 (C=O), 161.7 (C-7a), 169.5, 169.5, 170.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.78 (t, $^3J_{F,F}$ = 10.2 Hz, 3F, CF_3), -108.64 (q, $^3J_{F,F}$ = 10.2 Hz, 2F, CF_2), -124.24 (t, $^3J_{F,F}$ = 21.5 Hz, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2961 (w), 1747 (m), 1711 (w), 1583 (w), 1362 (m), 1222 (s), 1115 (m), 1043 (w), 1024 (w), 962 (w), 736 (m). MS (EI, 70 eV): *m/z* (%) = 872 (0.1) [M^++1], 871 (0.1) [M^+], 598 (12), 597 (14), 259 (63), 157 (16), 139 (100), 97 (31), 77 (8), 43 (39). HRMS (ESI): calcd $C_{44}H_{41}F_7N_3O_8$ ([M+1]$^+$) 872.27764, found 872.2777. Anal. Calcd for $C_{44}H_{40}F_7N_3O_8$: C, 60.62; H, 4.62; N, 4.82. Found: C, 60.42; H, 4.59; N, 4.85.

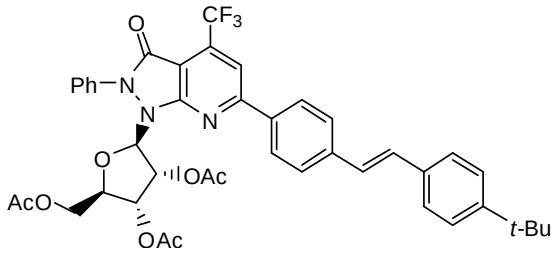
(*E*)-6-(4-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37p)



Starting from **9b** (614 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37p** was isolated as yellow foam (480 mg, 55%), mp 121-123 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9H, CH_3), 1.70 (s, 3H, OAc-5'), 2.11 (s, 3H, OAc-3'), 2.13 (s, 3H, OAc-2'), 3.82 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 5.0 Hz, 1H, H_a-5'), 4.04 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 3.4 Hz, 1H, H_b-5'), 4.07-4.12 (m, 1H, H-4'), 5.43 (t, $^3J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.64 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.65 (dd, $^3J_{H,H}$ = 6.4 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, H-2'), 7.14 (d, $^3J_{H,H}$ = 16.4 Hz, 1H, =CH), 7.28 (d, $^3J_{H,H}$ = 16.4 Hz, 1H, =CH), 7.33-7.38 (m, 1H, Ar), 7.43 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar), 7.48-7.53 (m, 4H, Ph), 7.61-7.65 (m, 2H, Ar), 7.72 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar), 7.92 (s, 1H, H-5), 8.27 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4, 20.6, 20.6 ($\underline{C}H_3CO$), 31.4 (CH_3), 34.9 ($\underline{C}(CH_3)_3$), 62.2 (CH_2), 69.4, 72.1, 78.4, 92.7 (CH_{rib}), 108.4 (C-3a), 114.9 (t, $^3J_{C,F}$ = 8.9 Hz, C-5), 124.8, 125.9, 126.7, 126.9, 127.5, 127.6, 128.5, 129.4, 131.0 (CH_{Ar}, =CH), 134.2, 134.9, 135.1 (C_{Ar}), 137.0 (t, $^2J_{C,F}$ = 26.3 Hz, $\underline{C}CF_2$), 141.1, 151.7, 158.1 (C_{Ar}), 160.6 (C=O), 161.2 (C-7a), 169.5, 169.6, 170.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.79 (t, $^3J_{F,F}$ = 10.2 Hz, 3F, CF_3), -108.72 (q, $^3J_{F,F}$ = 10.2 Hz, 2F, CF_2), -124.29 (t, $^3J_{F,F}$ = 20.4 Hz, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 871 (0.2) [M^+], 614 (45), 613 (94), 598 (28), 597 (47), 260 (22), 259 (61), 157 (58), 139 (100), 97 (64), 77 (49), 43 (99). HRMS (ESI): calcd $C_{44}H_{41}F_7N_3O_8$ ([M+1]$^+$) 872.27764, found 872.2777. Anal. Calcd for $C_{44}H_{40}F_7N_3O_8$: C, 60.62; H, 4.62; N, 4.82. Found: C, 60.87; H, 4.64; N, 4.88.

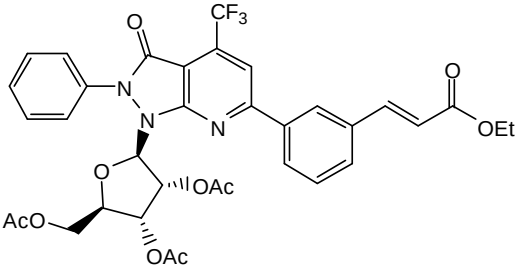
(*E*)-6-(4-(4-*tert*-butylstyryl)phenyl)-4-(trifluoromethyl)-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37q)



Starting from **9c** (513 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37q** was isolated as yellow foam (633 mg, 82%); mp 156-158 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (s, 9H, CH_3), 1.71 (s, 3H, OAc-5'), 2.10 (s, 3H, OAc-3'), 2.13 (s, 3H, OAc-2'), 3.82 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 5.0 Hz, 1H, H_a-5'), 4.02 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H_b-5'), 4.08-4.12 (m, 1H, H-4'), 5.43 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.63 (d, $^{3}J_{H,H}$ = 3.9 Hz, 1H, H-1'), 6.63 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 3.9 Hz, 1H, H-2'), 7.32-7.44 (m, 3H, Ar, =CH), 7.47-7.54 (m, 4H, Ar, =CH), 7.61-7.65 (m, 2H, Ar), 7.71 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar), 7.98 (s, 1H, H-5), 8.04 (s, 1H, Ar), 8.26 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4, 20.6, 20.6 ($\underline{C}H_3CO$), 31.4 (CH_3), 34.9 ($\underline{C}(CH_3)_3$), 62.2 (CH_2), 69.4, 72.1, 78.4, 92.7 (CH_{rib}), 108.6 (C-3a), 115.0 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 124.8, 125.9, 126.7, 126.9, 127.5, 127.6, 128.5, 129.4, 131.0 (CH_{Ar}, =CH), 134.2, 134.9, 135.1 (C_{Ar}), 137.0 (q, $^{2}J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 141.1, 151.7, 158.1 (C_{Ar}), 160.6 (C=O), 161.2 (C-7a), 169.5, 169.6, 170.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.87 (s). MS (EI, 70 eV): *m/z* (%) = 771 (0.1) [M^+], 513 (20), 498 (13), 260 (19), 259 (100), 97 (48), 77 (11), 44 (12), 43 (70). HRMS (ESI): calcd $C_{42}H_{41}F_3N_3O_8$ ([M+1]$^+$) 772.28403, found 772.28443.Anal. Calcd for $C_{42}H_{40}F_3N_3O_8$: C, 65.36; H, 5.22; N, 5.44. Found: C, 65.522; H, 5.198; N, 5.419.

(*E*)-Ethyl 3-(2-(3-oxo-2-phenyl-4-(trifluoromethyl)-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl)phenyl)acrylate (37r)

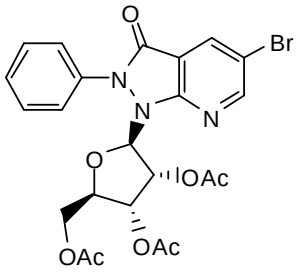


Starting from **11a** (453 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37r** was isolated as yellow foam (480 mg, 79%); mp 134-136 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.36 (t, $^{3}J_{H,H}$ = 7.1 Hz, 3H, CH_3), 1.72 (s, 3H, OAc-5'), 2.08 (s, 3H, OAc-3'), 2.12 (s, 3H, OAc-2'), 3.79 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 5.3 Hz, 1H, H_a-5'), 3.79 (dd, $^{2}J_{H,H}$ = 12.1 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H_b-5'), 4.06-4.13 (m, 1H, H-4'), 4.30 (q, $^{3}J_{H,H}$ = 7.1 Hz, 2H, OCH_2), 5.35 (t, $^{3}J_{H,H}$ = 6.3 Hz, 1H, H-3'), 5.67 (d, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-1'), 6.56 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, H-2'), 6.59 (d, $^{3}J_{H,H}$ = 16.1 Hz, 1H, =CH), 7.36 (tt, $^{3}J_{H,H}$ = 7.4 Hz, $^{4}J_{H,H}$ = 1.6 Hz, 1H, Ar), 7.48-7.54 (m, 2H, Ar), 7.59-7.65 (m, 3H, Ar), 7.75 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.86 (d, $^{3}J_{H,H}$ = 16.1 Hz,

1H, =CH), 7.98 (s, 1H, H-5), 8.26 (d, $^{3}J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.33 (br s, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.4, 20.5, 20.5 ($\underline{C}H_3CO$), 60.2, 62.2 (CH_2), 69.2, 72.0, 78.4, 92.4 (CH_{rib}), 103.4 (C-3a), 111.1 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 119.3 (=CH), 120.1 (CH_{Ar}), 122.0 (q, $^{1}J_{C,F}$ = 274.4 Hz, CF_3), 125.8, 127.5, 129.1, 129.3, 129.7, 130.6 (CH_{Ar}), 135.0 (C_{Ar}), 135.8 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 136.6, 137.4 (C_{Ar}), 143.7 (=CH), 155.4 (C_{Ar}), 157.5 (NC=O), 160.6 (C-7a), 166.2 ($\underline{C}O_2Et$), 169.4, 169.4, 170.3 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -61.76 (s). MS (EI, 70 eV): *m/z* (%) = 711 (0.12) [M^+], 453 (28), 260 (25), 259 (100), 97 (34), 77 (29), 44 (12), 43 (66). HRMS (ESI): calcd $C_{35}H_{33}F_3N_3O_{10}$ ($[M+1]^+$) 712.2139, found 712.2142. Anal. Calcd for $C_{35}H_{32}F_3N_3O_{10}$: C, 59.07; H, 4.53; N, 5.90. Found: C, 59.255; H, 4.551; N, 5.884.

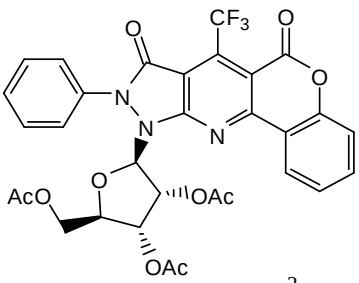
5-Bromo-2-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (37s)



Starting from **33a** (290 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37s** was isolated as pink foam (241 mg, 44%); mp 150-152 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3H, OAc-5'), 2.05 (s, 3H, OAc-3'), 2.09 (s, 3H, OAc-2'), 3.83-3.90 (m, 1H, H_a-5'), 4.02-4.10 (m, 2H, H_b-5', H-4'), 5.37 (t, $^{3}J_{H,H}$ = 5.9 Hz, 1H, H-3'), 5.60 (d, $^{3}J_{H,H}$ = 4.7 Hz, 1H, H-1'), 6.28 (dd, $^{3}J_{H,H}$ = 5.9 Hz, $^{3}J_{H,H}$ = 4.7 Hz, 1H, H-2'), 7.33-7.39 (m, 1H, Ar), 7.47-7.59 (m, 2H, Ar), 8.34 (d, $^{4}J_{H,H}$ = 2.3 Hz, 1H, H-4), 8.72 (d, $^{4}J_{H,H}$ = 2.3 Hz, 1H, H-6). Anal. Calcd for $C_{23}H_{22}BrN_3O_8$: C, 50.38; H, 4.04; N, 7.66. Found: C, 50.61; H, 4.12; N, 7.45.

9-Phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (37t)

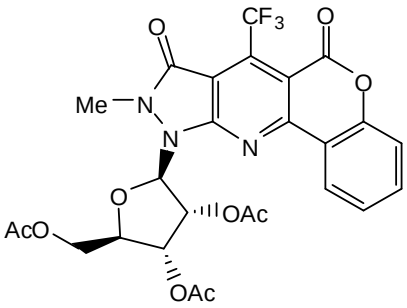


Starting from **22a** (397 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37t** was isolated as yellow foam (497 mg, 76%); mp 99-101 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (s, 3H, OAc-5'), 2.12 (s, 6H, OAc-2', OAc-3'), 3.88 (dd, $^{2}J_{H,H}$ = 12.2 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H_a-5'), 4.07 (dd, $^{2}J_{H,H}$ = 12.2 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H_b-5'), 4.11-4.17 (m, 1H, H-4'), 5.43 (dd, $^{3}J_{H,H}$ = 7.18 Hz, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.67 (d, $^{3}J_{H,H}$ = 3.8 Hz, 1H, H-1'), 6.57 (dd, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 3.8 Hz, 1H, H-2'), 7.39-7.44 (m, 2H, Ph), 7.47-7.61 (m, 5H, Ph), 7.68-7.74 (m, 1H, Ph), 8.75-8.79 (m, 1H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.6 ($\underline{C}H_3CO$), 62.2 (CH_2), 69.2, 71.7, 78.3, 92.7 (CH_{rib}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7

(C-6a), 121.1 (q, $^{1}J_{C,F}$ = 275.9 Hz, CF_3), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a), 169.5, 169.6, 170.3 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -56.84 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2944 (w), 1744 (m), 1713 (m), 1583 (m), 1494 (w), 1456 (w), 1366 (m), 1226 (s), 1156 (s), 1058 (m), 1041 (m), 1023 (m), 891 (m), 761 (m), 693 (m). MS (EI, 70 eV): *m/z* (%) = 656 (0.2) [M^++1], 655 (0.1) [M^+], 397 (31), 396 (17), 260 (23), 259 (100), 157 (30), 140 (16), 139 (88), 97 (82), 77 (58), 69 (13), 43 (72). HRMS (ESI): calcd $C_{31}H_{25}F_3N_3O_{10}$ ([M+1]$^+$) 656.14866, found 656.14851. Anal. Calcd for $C_{31}H_{24}F_3N_3O_{10}$: C, 56.80; H, 3.69; N, 6.41. Found: C, 57.15; H, 3.82; N, 6.27.

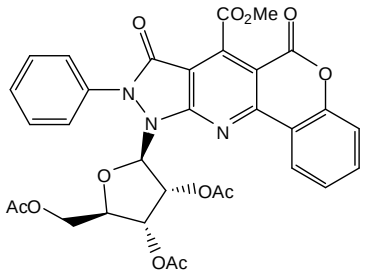
9-Methyl-7-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (37u)



Starting from **22b** (335 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37u** was isolated as yellow foam (404 mg, 68%); mp 125-126 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.81 (s, 3H, OAc-5'), 2.09 (s, 3H, OAc-2'), 2.17 (s, 3H, OAc-3'), 3.58 (s, 3H, NCH_3), 4.10 (dd, $^{2}J_{H,H}$ = 12.3 Hz, $^{3}J_{H,H}$ = 4.7 Hz, 1H, H_a-5'), 4.22-4.31 (m, 2H, H_b-5', H-4'), 5.55 (t, $^{3}J_{H,H}$ = 6.5 Hz, 1H, H-3'), 5.96 (d, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.38 (dd, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-2'), 7.38 (dd, $^{3}J_{H,H}$ = 8.3 Hz, $^{4}J_{H,H}$ = 0.8 Hz, 1H, Ar), 7.44-7.49 (m, 1H, Ar), 7.65-7.71 (m, 1H, Ar), 8.68 (dd, $^{3}J_{H,H}$ = 8.1 Hz, $^{4}J_{H,H}$ = 1.5 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.6 ($\underline{C}H_3CO$), 33.0 (NCH_3), 62.2 (CH_2), 69.2, 71.7, 78.3, 92.7 (CH_{rib}), 95.7 (C-7a), 117.6 (CH_{Ar}), 118.3 (C-6a), 121.1 (q, $^{1}J_{C,F}$ = 276.0 Hz, CF_3), 125.6, 126.4, 134.3 (CH_{Ar}), 143.9, 153.2, 155.9, 158.9 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a), 169.3, 170.2, 170.5 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -56.86 (s). MS (EI, 70 eV): *m/z* (%) = 593 (0.1) [M^+], 336 (28), 335 (21), 259 (100), 157 (61), 140 (22), 139 (94), 97 (79), 77 (36) 43 (62). HRMS (ESI): calcd $C_{26}H_{23}F_3N_3O_{10}$ ([M+1]$^+$) 594.12859, found 594.12854. Anal. Calcd for $C_{26}H_{22}F_3N_3O_{10}$: C, 52.62; H, 3.74; N, 7.08. Found: C, 53.01; H, 3.80; N, 6.92.

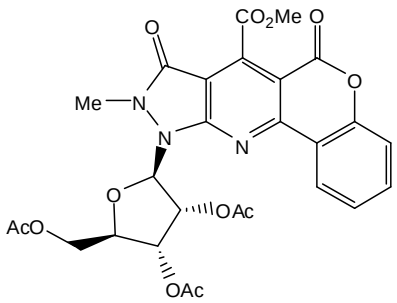
Methyl 6,8-dioxo-9-phenyl-1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-6,8,9,10-tetrahydro chromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (37v)



Starting from **22c** (387 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37v** was isolated as yellow foam (510 mg, 79%); mp 144-146 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 3H, OAc-5'), 2.12 (s, 3H, OAc-2'), 2.14 (s, 3H, OAc-3'), 3.86 (dd, $^{2}J_{H,H}$ = 12.0 Hz, $^{3}J_{H,H}$ = 5.2 Hz, 1H, H_a-5'), 4.06 (dd, $^{2}J_{H,H}$ = 12.0 Hz, $^{3}J_{H,H}$ = 5.2 Hz, 1H, H_b-5'), 4.10-4.16 (m, 1H, H-4'), 4.13 (s, 3H, OCH_3), 5.54 (t, $^{3}J_{H,H}$ = 6.7 Hz, 1H, H-3'), 5.61 (d, $^{3}J_{H,H}$ = 3.0 Hz, 1H, H-1'), 6.65 (br s, 1H, H-2'), 7.36-7.44 (m, 2H, Ph), 7.48-7.60 (m, 5H, Ph), 7.66-7.73 (m, 1H, Ph), 8.79-8.82 (m, 1H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.3, 20.5, 20.6 ($\underline{C}H_3CO$), 53.9 (OCH_3), 62.2 (CH_2), 69.2, 71.7, 78.3, 92.7 (CH_{rib}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 159.1 (CO-6), 159.3 (CO-8), 164.3 (C-10a), 169.5 ($\underline{C}O_2CH_3$), 170.0, 170.2, 170.3 ($\underline{C}OCH_3$). MS (EI, 70 eV): *m/z* (%) = 646 (0.3) [M^++1], 645 (0.1) [M^+], 387 (89), 356 (13), 329 (32), 300 (14), 260 (15), 259 (88), 157 (22), 156 (18), 140 (13), 139 (87), 115 (21), 97 (68), 85 (35), 77 (43), 69 (20), 43 (100). HRMS (ESI): calcd $C_{32}H_{28}N_3O_{12}$ ([M+1]$^+$) 646.16675, found 646.16614. Anal. Calcd for $C_{32}H_{27}N_3O_{12}$: C, 59.54; H, 4.22; N, 6.51. Found: C, 59.69; H, 4.41; N, 6.20.

Methyl 1-(2,3,5-tri-O-acetyl-β-D-ribofuranozyl)-9-methyl-6,8-dioxo-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (37w)

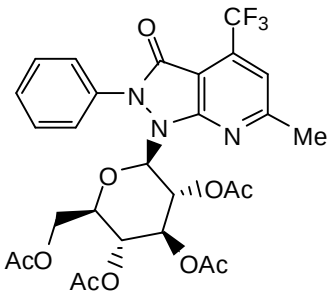


Starting from **22d** (325 mg, 1 mmol) and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (318 mg, 1mmol), **37w** was isolated as yellow foam (473 mg, 81%); mp 100-101 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 3H, OAc-5'), 2.12 (s, 3H, OAc-2'), 2.17 (s, 3H, OAc-3'), 3.55 (s, 3H, NCH_3), 4.04 (dd, $^{2}J_{H,H}$ = 12.3 Hz, $^{3}J_{H,H}$ = 4.9 Hz, 1H, H_a-5'), 4.15 (s, 3H, CO_2CH_3), 4.06 (dd, $^{2}J_{H,H}$ = 12.3 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, H_b-5'), 4.27-4.32 (m, 1H, H-4'), 5.65 (t, $^{3}J_{H,H}$ = 6.4 Hz, 1H, H-3'), 5.86 (d, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-1'), 6.52 (dd, $^{2}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.3 Hz, 1H, H-2'), 7.38-7.41 (m, 1H, Ar), 7.45-7.50 (m, 1H, Ar), 7.64-7.69 (m, 1H, Ar), 8.71-8.75 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): 20.5, 20.6 ($\underline{C}H_3CO$), 31.0 (NCH_3), 53.9 (OCH_3), 62.4 (CH_2), 69.3, 71.8, 78.7, 90.4 (CH_{Rib}), 109.5 (C-7a), 117.6 (CH_{Ar}), 118.3 (C-6a), 125.6, 126.4, 134.3 (CH_{Ar}), 143.9, 153.2, 155.9, 158.9 (C_{Ar}), 159.1 (CO-6), 159.3 (CO-8), 164.3 (C-10a), 169.5 ($\underline{C}O_2CH_3$), 169.6, 170.3 ($CH_3\underline{C}O$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2953

(w), 1738 (m), 1732 (m), 1694 (w), 1607 (w), 1592 (w), 1435 (w), 1396 (m), 1269 (m), 1220 (s), 1156 (w), 1136 (w), 1092 (w), 1042 (m), 1031 (m), 897 (w), 762 (m). MS (EI, 70 eV): *m/z* (%) = 583 (0.1) [M^+], 325 (100), 310 (57), 265 (24), 259 (86), 157 (41), 101 (74), 96 (45), 85 (21), 73 (21), 57 (41), 43 (100). HRMS (ESI): calcd $C_{27}H_{26}N_3O_{12}$ ([M+1]$^+$) 584.1511, found 584.15099. Anal. Calcd for $C_{27}H_{25}N_3O_{12}$: C, 55.58; H, 4.32; N, 7.20. Found: C, 55.934; H, 4.531; N, 6.992.

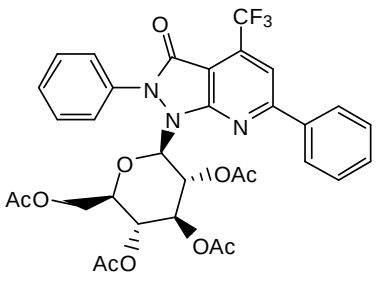
6-Methyl-2-phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38a)



Starting from **2a** (293 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38a** was isolated as yellow foam (474 mg, 76%); mp 96-97 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 3H, OAc-6'), 1.97 (s, 6H, OAc-4', OAc-3'), 1.98 (s, 3H, OAc-2'), 2.79 (s, 3H, CH_3), 3.99-4.09 (m, 3H, H_a-6', H_b-6', H-5'), 4.93 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-4'), 5.13 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-3'), 5.44-5.50 (m, 1H, H-2'), 5.94 (br s, 1H, H-1'), 7.32-7.37 (m, 1H, Ph), 7.33 (s, 1H, H-5), 7.44-7.49 (m, 2H, Ph), 7.52-7.57 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.1, 20.5, 20.5, 20.6 (CO$\underline{C}H_3$), 25.4 (CH_3), 61.5 (CH_2), 67.6, 69.2, 73.8, 74.3, 86.8 (CH_{gl}), 104.5 (C- 3a), 116.1 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.4 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 125.2, 127.6, 128.9 (CH_{Ar}), 135.1 (C_{Ar}), 136.3 (q, $^2J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 158.3 (C-6), 160.3 (C=O), 165.6 (C-7a), 168.3, 169.3, 170.3, 170.3 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.76 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2943 (w), 1750 (m), 1710 (m), 1593 (m), 1489 (w), 1363 (m), 1208 (s), 1144 (m), 1032 (s), 896 (m), 750 (m), 702 (m), 598 (m). MS (EI, 70 eV): *m/z* (%) = 624 (0.28) [M^+], 331 (50), 293 (31), 169 (100), 127 (25), 109 (83), 77 (14), 43 (84). HRMS (ESI): calcd $C_{28}H_{29}F_3N_3O_{10}$ ([M+1]$^+$) 624.18, found 624.1805. Anal. Calcd for $C_{28}H_{28}F_3N_3O_{10}$: C, 53.93; H, 4.53; N, 6.74. Found: C, 54.06; H, 4.47; N, 6.69.

2,6-Biphenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38b)

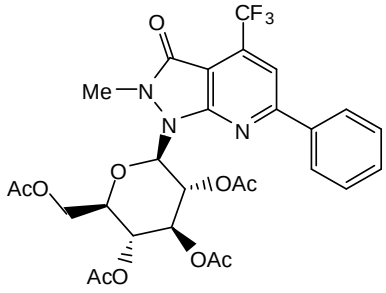


Starting from **2c** (355 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38b** was isolated as yellow foam (548 mg, 80%); mp 122-123 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84 (s, 3H, OAc-6'), 1.91 (s, 3H, OAc-4'), 1.94 (s, 3H, OAc-3'), 1.96 (s, 3H, OAc-2'), 3.61

(br s, 1H, H-5'), 3.91-4.08 (m, 3H, H_a-6', H_b-6', H-4'), 4.86-4.92 (m, 1H, H-3'), 5.04-5.22 (m, 2H, H-2', H-1'), 7.31 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, Ph), 7.43 (t, $^3J_{H,H}$ = 7.5 Hz, 2H, Ph), 7.51-7.53 (m, 5H, Ph), 7.87 (s, 1H, H-5), 8.14-8.17 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.2, 20.5, 20.5, 20.5 ($CO\underline{C}H_3$), 61.5 (CH_2), 67.7, 69.4, 73.9, 74.3, 86.8 (CH_{gl}), 106.0 (C-3a), 113.1 (C-5), 121.5 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 125.0, 127.6, 127.9, 129.1, 129.3, 131.4 (CH_{Ar}), 136.7 (C_{Ar}), 137.1 (q, $^2J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 158.2 (C-6), 160.6 (C=O), 162.5 (C-7a), 168.4, 169.2, 170.2, 170.3 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.69 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2969 (w), 2950 (w), 1740 (s), 1592 (w), 1368 (m), 1217 (s), 1154 (m), 1065 (s), 1032 (s), 902 (m). MS (EI, 70 eV): *m/z* (%) = 686 (0.4) [M^+], 355 (46), 331 (79), 271 (11), 169 (100), 127 (40), 109 (88), 77 (28), 43 (92). HRMS (ESI): calcd $C_{33}H_{31}F_3N_3O_{10}$ ([M+1]$^+$) 686.1956, found 686.1953. Anal. Calcd for $C_{33}H_{30}F_3N_3O_{10}$: C, 57.81; H, 4.41; N, 6.13. Found: C, 57.87; H, 4.37; N, 6.18.

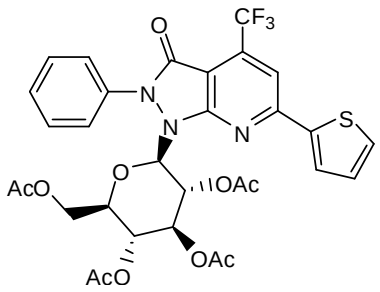
2-Methyl-6-phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38c)



Starting from **2d** (293 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38c** was isolated as colorless foam (486 mg, 78%); mp 99-101 °C.

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.44 (s, 3H, OAc-6'), 1.92 (s, 3H, OAc-4'), 1.99 (s, 3H, OAc-3'), 2.00 (s, 3H, OAc-2'), 3.52 (s, 3H, NCH_3), 3.87-3.93 (m, 1H, H-5'), 4.09-4.26 (m, 2H, H_a-6', H_b-6'), 5.15 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-4'), 5.27 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-3'), 5.48 (br s, 1H, H-2'), 5.93 (d, $^3J_{H,H}$ = 9.3 Hz, 1H, H-1'), 7.48-7.55 (m, 3H, Ph), 7.75 (s, 1H, H-5), 8.03-8.08 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.6, 20.5, 20.5, 20.6 ($\underline{C}H_3CO$), 33.0 (NCH_3), 61.6 (CH_2), 67.7, 69.0, 73.4, 74.8, 85.9 (CH_{gl}), 104.7 (C-8), 112.1 (q, $^3J_{C,F}$ = 4.9 Hz, C-5), 121.5 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 127.8, 129.2, 131.3 (CH_{Ar}), 136.7 (q, $^2J_{C,F}$ = 36.5 Hz, $\underline{C}CF_3$), 136.7 (C_{Ar}), 159.4 (C-6), 159.5 (CO), 162.0 (C-9), 168.2, 169.3, 170.1, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, CDCl3): δ = -62.69 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2960 (w), 1748 (m), 1695 (m), 1595 (m), 1443 (w), 1410 (w), 1372 (m), 1213 (s), 1149 (m), 1031 (s), 776 (m), 692 (m). MS (EI, 70 eV): *m/z* (%) = 624 (0.24) [M^+], 331 (36), 293 (29), 169 (100), 127 (20), 109 (71), 43 (79). HRMS (ESI): calcd $C_{28}H_{29}F_3N_3O_{10}$ ([M+1]$^+$) 624.17996, found 624.18007. Anal. Calcd for $C_{28}H_{28}F_3N_3O_{10}$: C, 53.93; H, 4.53; N, 6.74. Found: C, 54.16; H, 4.72; N, 6.75.

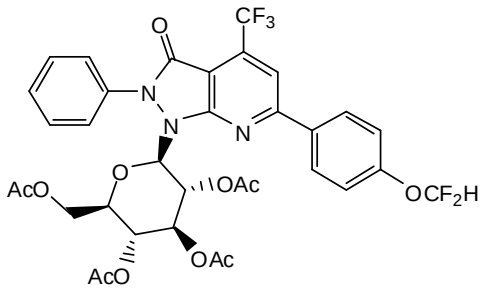
2-Phenyl-6-(thiophen-2-yl)-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38e)



Starting from **2g** (361 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38e** was isolated as colorless foam (595 mg, 86%); mp 151-153 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84 (s, 3H, OAc-6'), 1.91 (s, 3H, OAc-4'), 1.94 (s, 3H, OAc-3'), 1.96 (s, 3H, OAc-2'), 3.61 (br s, 1H, H-5'), 3.91-4.08 (m, 3H, H_a-6', H_b-6', H-4'), 4.86-4.92 (m, 1H, H-3'), 5.04-5.22 (m, 2H, H-2', H-1'), 7.23 (dd, $^3J_{H,H}$ = 4.9 Hz, $^3J_{H,H}$ = 3.8 Hz, 1H, Hetar), 7.34-7.39 (m, 1H, Ar), 7.47-7.52 (m, 2H, Ar), 7.55-7.58 (m, 2H, Ar), 7.65 (dd, $^2J_{H,H}$ = 4.9 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Hetar), 7.77 (s, 1H, H-5), 7.91 (dd, $^3J_{H,H}$ = 3.8 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.1 (CH_3), 20.2, 20.7, 20.8 ($\underline{C}H_3CO$), 32.1 ($N\underline{C}H_3$), 66.7, 69.0, 71.8, 72.8, 80.3 (CH_{gl}), 105.6 (C-8), 111.9 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 127.6, 129.1, 131.1 (CH_{Ar}), 136.6 (q, $^2J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 136.9 (C_{Ar}), 159.3 (C-6), 159.7 (CO), 161.4 (C-9), 168.9, 169.0, 169.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.87 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3106 (w), 2956 (w), 1756 (m), 1715 (m), 1589 (m), 1536 (w), 1493 (w), 1426 (m), 1377 (m), 1210 (s), 1155 (m), 1060 (m), 1034 (s), 953 (w), 907 (w), 706 (w). MS (EI, 70 eV): *m/z* (%) = 692 (0.5) [M^++1], 691 (0.1) [M^+], 362 (20), 361 (53), 360 (17), 332 (25), 331 (89), 170 (18), 169 (100), 127 (38), 109 (91), 97 (10), 77 (27), 43 (76). HRMS (ESI): calcd $C_{31}H_{29}F_3N_3O_{10}S$ ([M+1]$^+$) 692.15203, found 692.15251. Anal. Calcd for $C_{31}H_{28}F_3N_3O_{10}S$: C, 53.83; H, 4.08; N, 6.08. Found: C, 54.12; H, 4.18; N, 5.94.

6-(4-(Difluoromethoxy)phenyl)-2-phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38g)

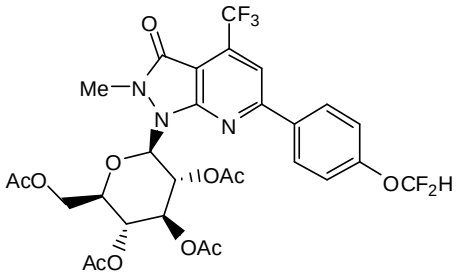


Starting from **2r** (421 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38g** was isolated as colorless foam (556 mg, 74%); mp 100-102 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.84 (s, 3H, OAc-6'), 1.91 (s, 3H, OAc-4'), 1.94 (s, 3H, OAc-3'), 1.96 (s, 3H, OAc-2'), 3.58 (br s, 1H, H-5'), 3.94-3.95 (m, 2H, H_a-6', H_b-6'), 4.87-4.93 (m, 1H, H-4'), 5.03-5.22 (m, 2H, H-3', H-2'), 5.65 (d, $^3J_{H,H}$ = 8.3 Hz, 1H, H-1'), 6.59 (t, $^2J_{F,H}$ = 73.3 Hz, 1H, OCF_2H), 7.27-7.34 (m, 3H, Ar), 7.41-7.47 (m, 2H, Ar), 7.50-7.53 (m, 2H, Ar), 7.82 (s, 1H, H-5), 8.17-8.20 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.7

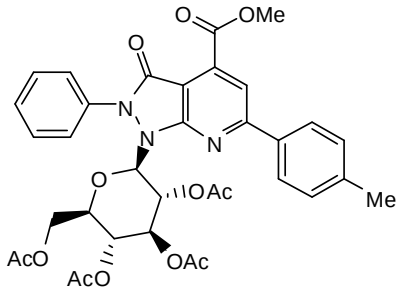
(CO<u>C</u>H$_3$), 61.4 (CH_2), 67.8, 70.2, 72.7, 74.3, 91.7 (CH_{gl}), 111.4 (C-3a), 112.9 (C-5), 115.6 (t, $^1J_{C,F}$ = 260.9 Hz, OCF_2H), 119.8 (CH_{Ar}), 121.4 (q, $^1J_{C,F}$ = 275.0 Hz, CF_3), 124.9, 127.7, 129.2, 129.8 (CH_{Ar}), 133.8 (C_{Ar}), 137.2 (q, $^2J_{C,F}$ = 36.5 Hz, <u>C</u>CF_3), 153.6 (t, $^3J_{C,F}$ = 2.8 Hz, <u>C</u>OCF_2H), 158.0, 160.5 (C_{Ar}), 161.2 (C=O), 168.5 (C-7a), 168.9, 169.3, 170.0, 170.5 (<u>C</u>OCH_3). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -81.38 (s, 2F, OCF_2H), -62.68 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3069 (w), 2943 (w), 1748 (m), 1705 (m), 1593 (m), 1494 (w), 1368 (m), 1210 (s), 1115 (m), 1030 (s), 904 (w), 841 (w), 596 (w). MS (EI, 70 eV): *m/z* (%) = 752 (0.48) [M^+], 732 (2), 421 (61), 331 (100), 271 (27), 169 (99), 127 (70), 109 (99), 77 (49), 43 (92). HRMS (ESI): calcd $C_{34}H_{31}F_5N_3O_{11}$ ([M+1]$^+$) 752.1873, found 752.1884. Anal. Calcd for $C_{34}H_{30}F_5N_3O_{11}$: C, 54.33; H, 4.02; N, 5.59. Found: C, 54.67; H, 3.96; N, 5.44.

6-(4-(Difluoromethoxy)phenyl)-2-methyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38h)



Starting from **2s** (359 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38h** was isolated as yellow foam (476 mg, 69%); mp 89-91 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47 (s, 3H, OAc-6'), 1.93 (s, 3H, OAc-4'), 1.99 (s, 6H, OAc-3', OAc-2'), 3.52 (s, 3H, NCH_3), 3.86-3.92 (m, 1H, H-5'), 4.12 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 2.0 Hz, 1H, H_a-6'), 4.22 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 4.3 Hz, 1H, H_b-6'), 5.14 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-4'), 5.28 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-3'), 5.55 (br s, 1H, H-2'), 5.85 (br s, 1H, H-1'), 6.57 (t, $^2J_{H,F}$ = 73.2 Hz, 1H, OCF_2H), 7.23-7.26 (m, 2H, Ar), 7.71 (s, 1H, H-5), 8.08-8.11 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.7, 20.5, 20.6 (CO<u>C</u>H_3), 32.9 (NCH_3), 61.6 (CH_2), 67.7, 69.0, 73.4, 74.8, 85.8 (CH_{gl}), 111.3 (C-3a), 111.7 (C-5), 115.5 (t, $^1J_{C,F}$ = 261.4 Hz, OCF_2H), 119.8 (CH_{Ar}), 121.4 (q, $^1J_{C,F}$ = 274.4 Hz, CF_3), 129.5 (CH_{Ar}), 133.7 (C_{Ar}), 136.9 (q, $^2J_{C,F}$ = 36.6 Hz, <u>C</u>CF_3), 153.5 (t, $^3J_{C,F}$ = 2.7 Hz, <u>C</u>OCF_2H), 159.3 (C_{Ar}), 159.4 (C=O), 160.7 (C-7a), 168.3, 169.3, 170.2, 170.5 (<u>C</u>OCH_3). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -81.48 (s, 2F, OCF_2H), -62.70 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2964 (w), 1754 (m), 1717 (m), 1586 (m), 1500 (w), 1371 (m), 1214 (s), 1117 (s), 1023 (s), 917 (m), 881 (m), 782 (m), 674 (m). MS (EI, 70 eV): *m/z* (%) = 690 (0.7) [M^+], 359 (93), 331 (100), 169 (100), 139 (42), 127 (89), 109 (100), 97 (42), 43 (100). HRMS (ESI): calcd $C_{29}H_{29}F_5N_3O_{11}$ ([M+1]$^+$) 690.17168, found 690.17333. Anal. Calcd for $C_{29}H_{28}F_5N_3O_{11}$: C, 50.51; H, 4.09; N, 6.09. Found: C, 50.77; H, 4.37; N, 6.36.

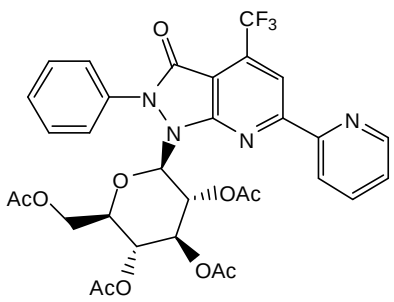
Methyl 3-oxo-2-phenyl-6-*p*-tolyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (38i)



Starting from **2u** (359 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38i** was isolated as yellow foam (648 mg, 94%); mp 101-103 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (s, 3H, OAc-6'), 1.99 (s, 6H, OAc-4', OAc-3'), 1.99 (s, 3H, OAc-2'), 2.47 (s, 3H, CH_3), 3.67 (br s, 1H, H-5'), 3.96-4.01 (m, 2H, H_a-6', H_b-6'), 4.03 (s, 3H, OMe), 4.93 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-4'), 5.15 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-3'), 5.53 (br s, 1H, H-2'), 5.89 (br s, 1H, H-1'), 7.33-7.40 (m, 3H, Ar), 7.46-7.51 (m, 2H, Ar), 7.56-7.59 (m, 2H, Ar), 7.95 (s, 1H, H-5), 8.11-8.14 (m, 2H, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): 20.4, 20.6, 20.7, 20.7 ($CO\underline{C}H_3$), 31.6 (CH_3), 53.3 (OCH_3), 61.6 (CH_2), 67.9, 69.5, 74.1, 74.4, 87.1 (CH_{gl}), 106.4 (C-3a), 116.1 (C-5), 125.3, 127.6, 127.9, 129.1, 130.1 (CH_{Ar}), 134.4, 139.4, 141.7, 145.6, 159.6 (C_{Ar}), 160.6 (C=O), 162.1 (C-7a), 165.4 ($\underline{C}O_2CH_3$), 168.6, 169.4, 170.4, 170.5 ($CH_3\underline{C}O$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2952 (w), 2922 (w), 2853 (w), 1744 (m), 1705 (m), 1583 (m), 1362 (m), 1209 (s), 1033 (s), 904 (w), 825 (w), 761 (w), 736 (w), 597 (w). MS (EI, 70 eV): *m/z* (%) = 689 (1.2) [M^+], 359 (29), 331 (50), 169 (100), 127 (18), 109 (69), 77 (7), 43 (69). HRMS (ESI): calcd $C_{35}H_{36}N_3O_{12}$ ([M+1]$^+$) 690.2294, found 690.2292. Anal. Calcd for $C_{35}H_{35}N_3O_{12}$: C, 60.95; H, 5.12; N, 6.09. Found: C, 61.17; H, 5.09; N, 5.98.

2-Phenyl-6-(pyridin-2-yl)-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (38l)

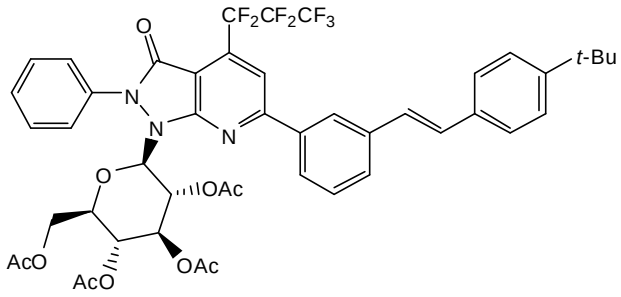


Starting from **2x** (356 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38l** was isolated as yellow foam (467 mg, 68%); mp 88-90 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (s, 3H, OAc-6'), 1.97 (s, 3H, OAc-4'), 1.98 (s, 3H, OAc-3'), 1.99 (s, 3H, OAc-2'), 3.70-3.74 (m, 1H, H-5'), 4.02 (d, $^3J_{H,H}$ = 3.2 Hz, 2H, H_a-6', H_b-6'), 4.90 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-4'), 5.18 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 5.94 (br s, 1H, H-1'), 7.37-7.45 (m, 2H, Ar), 7.48-7.53 (m, 2H, Ar), 7.56-7.59 (m, 2H, Ar), 7.85 (td, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.7 Hz, 1H, Ar), 8.28 (s, 1H, H-5), 8.50 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 7.85 (ddd, $^3J_{H,H}$ = 4.7 Hz, $^4J_{H,H}$ = 1.7 Hz, $^4J_{H,H}$ = 0.9 Hz, 1H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.3, 20.6, 20.7, 20.7 ($CO\underline{C}H_3$), 61.4 (CH_2), 67.6, 69.3, 73.8, 74.4, 87.3 (CH_{gl}), 113.5 (C-3a), 117.1 (C-5), 121.1 (q, $^1J_{C,F}$ = 275.1 Hz, CF_3), 125.5, 126.0, 127.7, 128.3,

129.2, 137.4, 149.5 (CH_{Ar}), 149.9, 150.0 (C_{Ar}), 151.4 (q, $^2J_{C,F}$ = 35.8 Hz, $\underline{C}CF_3$), 157.5 (C_{Ar}), 159.7 (C=O), 159.9 (C-7a), 168.4, 169.3, 170.4, 170.5 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -67.78 (s). MS (EI, 70 eV): *m/z* (%) = 687 (0.24) [M+1], 686 (0.13) [M^+], 356 (20), 331 (28), 169 (100), 157 (16), 127 (16), 115 (28), 109 (45), 98 (17), 43 (100). HRMS (ESI): calcd $C_{32}H_{30}F_3N_4O_{10}$ ([M+1]$^+$) 687.19085, found 687.1915. Anal. Calcd for $C_{32}H_{29}F_3N_4O_{10}$: C, 55.98; H, 4.26; N, 8.16. Found: C, 55.82; H, 4.21; N, 8.19.

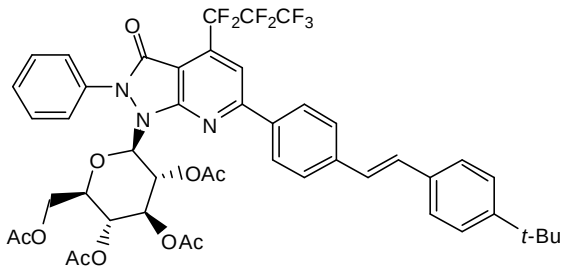
(*E*)-6-(3-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38o)



Starting from **9a** (614 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38o** was isolated as yellow foam (670 mg, 71%); mp 99-100 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.73 (s, 3H, OAc-6'), 1.97 (s, 3H, OAc-4'), 1.98 (s, 3H, OAc-3'), 1.99 (s, 3H, OAc-2'), 3.70-3.74 (m, 1H, H-5'), 4.02 (d, $^3J_{H,H}$ = 3.2 Hz, 2H, H_a-6', H_b-6'), 4.90 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-4'), 5.18 (t, $^3J_{H,H}$ = 9.4 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 5.94 (br s, 1H, H-1'), 7.28 (d, $^3J_{H,H}$ = 16.4 Hz, 1H, =CH), 7.33-7.38 (m, 1H, Ar), 7.43 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar), 7.48-7.53 (m, 4H, Ph), 7.61-7.65 (m, 2H, Ar), 7.72 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar), 7.92 (s, 1H, H-5), 8.27 (d, $^3J_{H,H}$ = 8.3 Hz, 2H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.4, 20.6, 20.6 ($\underline{C}H_3CO$), 31.4 (CH_3), 34.9 ($\underline{C}(CH_3)_3$), 62.2 (CH_2), 69.4, 72.1, 78.4, 92.7 (CH_{gl}), 108.4 (C-3a), 114.9 (t, $^3J_{C,F}$ = 8.9 Hz, C-5), 124.8, 125.9, 126.7, 126.9, 127.5, 127.6, 128.5, 129.4, 131.0 (CH_{Ar}, =CH), 134.2, 134.9, 135.1 (C_{Ar}), 137.0 (t, $^2J_{C,F}$ = 26.3 Hz, $\underline{C}CF_2$), 141.1, 151.7, 158.1 (C_{Ar}), 160.6 (C=O), 161.2 (C-7a), 169.5, 169.6, 170.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.79 (t, $^3J_{F,F}$ = 10.2 Hz, 3F, CF_3), -108.76 (br s, 2F, CF_2), -124.24 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 1755 (m), 1714 (w), 1584 (w), 1495 (w), 1434 (w), 1363 (m), 1271 (w), 1209 (s), 1147 (w), 1116 (m), 1034 (m), 953 (m), 906 (w), 737 (w), 691 (w), 597 (w). (EI, 70 eV): *m/z* (%) = 944 (1.1) [M^++1], 943 (1.3) [M^+], 614 (37), 613 (69), 612 (38), 598 (54), 597 (34), 332 (44), 331 (93), 271 (60), 211 (30), 170 (67), 169 (100), 145 (30), 139 (27), 127 (72), 110 (93), 97 (20), 77 (35), 43 (94). HRMS (ESI): calcd $C_{47}H_{45}F_7N_3O_{10}$ ([M+1]$^+$) 944.29877, found 944.29898. Anal. Calcd for $C_{47}H_{44}F_7N_3O_{10}$: C, 59.81; H, 4.70; N, 4.45. Found: C, 59.71; H, 4.72; N, 4.42.

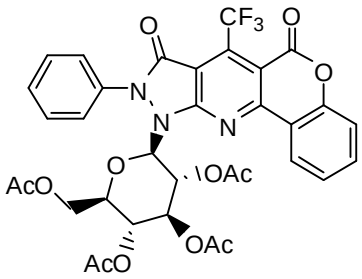
(*E*)-6-(4-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (38p)



Starting from **9b** (614 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38p** was isolated as yellow foam (585 mg, 62%); mp 124-126 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (s, 3H, OAc-6'), 1.36 (s, 9H, CH_3), 1.92 (s, 3H, OAc-4'), 1.99 (s, 3H, OAc-3'), 2.02 (s, 3H, OAc-2'), 3.69 (br s, 1H, H-5'), 3.99-4.05 (m, 2H, H_a-6', H_b-6'), 4.97 (br s, H-4'), 5.18 (t, $^{3}J_{H,H}$ = 9.4 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 5.94 (br s, 1H, H-1'), 7.17 (d, $^{3}J_{H,H}$ = 16.2 Hz, 1H, =CH), 7.32-7.60 (m, 10H, Ar), 7.75 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar), 7.89 (s, 1H, H-5), 8.24 (d, $^{3}J_{H,H}$ = 8.5 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.7, 20.7, 20.8 ($\underline{C}H_3CO$), 31.4 (CH_3), 34.9 ($\underline{C}(CH_3)_3$), 61.7 (CH_2), 68.0, 74.1, 74.5, 93.2 (CH_{gl}), 109.1 (C-3a), 115.1 (C-5), 125.3, 125.9, 126.7, 126.9, 127.4, 127.8, 128.5, 129.2, 131.0 (CH_{Ar}, =CH), 134.3, 135.3, 135.4, 141.0, 151.7, 159.1 (C_{Ar}), 160.7 (C=O), 161.6 (C-7a), 169.4, 170.4, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.79 (t, $^{3}J_{F,F}$ = 10.2 Hz, 3F, CF_3), -108.76 (br s, 2F, CF_2), -124.24 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2958 (w), 1755 (m), 1715 (m), 1582 (m), 1495 (w), 1417 (w), 1365 (m), 1211 (s), 1183 (m), 1148 (m), 1116 (m), 1033 (m), 954 (m), 903 (w), 837 (m), 736 9m), 561 (m). MS (EI, 70 eV): *m/z* (%) = 943 (0.4) [M^+], 614 (17), 613 (46), 599 (12), 598 (41), 455 (16), 369 (72), 331 (66), 318 (24), 317 (100), 287 (17), 271 (18), 205 (20), 203 (20), 170 (16), 169 (78), 127 (23), 109 (82), 77 (27), 44 (43), 43 (88), 41 (12). HRMS (ESI): calcd $C_{47}H_{45}F_7N_3O_{10}$ ([M+1]$^+$) 944.29877, found 944.29642.Anal. Calcd for $C_{47}H_{44}F_7N_3O_{10}$: C, 59.81; H, 4.70; N, 4.45. Found: C, 59.62; H, 4.67; N, 4.49.

9-Phenyl-1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (38t)

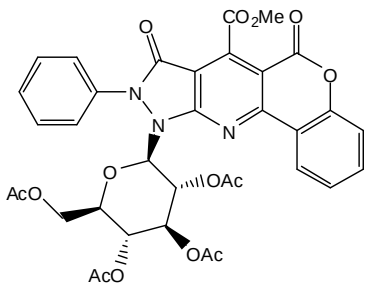


Starting from **22a** (397 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38t** was isolated as yellow foam 473 mg (65%); mp 89-91 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3H, OAc-6'), 1.93 (s, 3H, OAc-4'), 2.01 (s, 3H, OAc-3'), 2.03 (s, 3H, OAc-2'), 3.70 (br m, 1H, H-5') 4.06-4.07 (m, 2H, H_a-6', H_b-6'), 5.03 (br m, 1H, H-4'), 5.19 (t, $^{3}J_{H,H}$ = 9.4 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 5.98 (br s, 1H, H-1'), 7.40-

7.57 (m, 7H, Ar), 7.70-7.76 (m, 1H, Ar), 8.72 (d, $^{3}J_{H,H}$ = 7.6 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.7, 20.5, 20.6 ($CO\underline{C}H_3$), 61.6 (CH_2), 67.7, 69.0, 73.4, 74.8, 85.8 (CH_{gl}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 121.1 (q, $^{1}J_{C,F}$ = 276.0 Hz, CF_3), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a), 168.3, 169.3, 170.2, 170.5 ($\underline{C}OCH_3$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -56.86 (s). MS (EI, 70 eV): *m/z* (%) = 728 (0.3) [M^++1], 727 (0.1) [M^+], 398 (37), 397 (92), 396 (32), 377 (44), 332 (34), 331 (99), 271 (29), 170 (69), 169 (100), 145 (38), 139 (45), 127 (89), 115 (20), 110 (30), 109 (100), 98 (23), 97 (59), 85 (16), 81 (34), 77 (88), 69 (12), 60 (13), 43 (99). HRMS (ESI): calcd $C_{34}H_{29}F_3N_3O_{12}$ ([M+1]$^+$) 728.16978, found 728.16907. Anal. Calcd for $C_{34}H_{28}F_3N_3O_{12}$: C, 56.13; H, 3.88; N, 5.78. Found: C, 56.40; H, 4.00; N, 5.45.

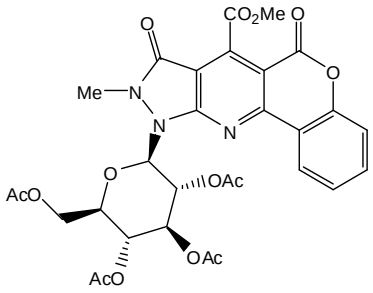
Methyl 1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-6,8-dioxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (38v)



Starting from **22c** (387 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38v** was isolated as yellow foam (524 mg, 73%); mp 142-144 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (s, 3H, OAc-6'), 2.02 (s, 3H, OAc-4'), 2.07 (s, 6H, OAc-3', OAc-2'), 3.96-4.01 (m, 1H, H-5'), 4.22 (dd, $^{2}J_{H,H}$ = 12.5 Hz, $^{3}J_{H,H}$ = 2.1 Hz, 1H, H_a-6'), 4.34 (dd, $^{2}J_{H,H}$ = 12.5 Hz, $^{3}J_{H,H}$ = 4.4 Hz, 1H, H_b-6'), 5.24 (t, $^{3}J_{H,H}$ = 9.6 Hz, 1H, H-4'), 5.37 (t, $^{3}J_{H,H}$ = 9.6 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 6.00 (d, $^{3}J_{H,H}$ = 7.9 Hz, 1H, H-1'), 7.40-7.57 (m, 7H, Ar), 7.70-7.76 (m, 1H, Ar), 8.72 (d, $^{3}J_{H,H}$ = 7.6 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 19.7, 20.5, 20.6 ($CO\underline{C}H_3$), 53.2 (OCH_3), 61.6 (CH_2), 67.7, 69.0, 73.4, 74.8, 85.8 (CH_{gl}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a), 168.5 ($\underline{C}O_2CH_3$), 169.3, 170.2, 170.5 ($\underline{C}OCH_3$). Anal. Calcd for $C_{35}H_{31}N_3O_{14}$: C, 58.58; H, 4.35; N, 5.86. found: C, 58.76; H, 4.61; N, 5.54.

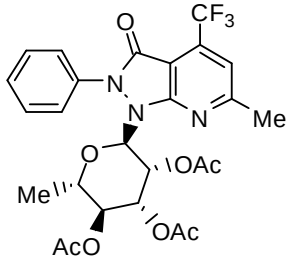
Methyl 1-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranozyl)-9-methyl-6,8-dioxo-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (38w)



Starting from **22d** (325 mg, 1 mmol) and 1,2,3,4,6-penta-O-acetyl-β-D-glucose (390 mg, 1mmol), **38w** was isolated as yellow foam (373 mg, 57%); mp 99-101 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 3H, OAc-6'), 2.01 (s, 3H, OAc-4'), 2.07 (s, 6H, OAc-3', OAc-2'), 3.58 (s, 3H, NCH_3), 3.97-4.03 (m, 1H, H-5'), 4.13 (s, 3H, OCH_3), 4.20 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H_a-6'), 4.31 (dd, $^2J_{H,H}$ = 12.5 Hz, $^3J_{H,H}$ = 4.4 Hz, 1H, H_b-6'), 5.24 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-4'), 5.37 (t, $^3J_{H,H}$ = 9.6 Hz, 1H, H-3'), 5.62 (br s, 1H, H-2'), 6.00 (d, $^3J_{H,H}$ = 7.9 Hz, 1H, H-1'), 7.39-7.42 (m, 1H, Ar), 7.47-7.52 (m, 1H, Ar), 7.66-7.72 (m, 1H, Ar), 8.62-8.65 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.0, 20.7, 20.8 ($CO\underline{C}H_3$), 33.0 (NCH_3), 53.9 (OCH_3), 61.6 (CH_2), 67.7, 69.0, 73.4, 75.2, 85.7 (CH_{gl}), 109.3 (C-7a), 117.6 (CH_{Ar}), 118.2 (C-6a), 125.4, 126.2, 134.4 (CH_{Ar}), 134.7, 153.3, 156.1, 158.8 (C_{Ar}), 159.4 (CO-6), 159.7 (CO-8), 164.2 (C-10a), 168.5 ($\underline{C}O_2CH_3$), 169.4, 170.3, 170.6 ($\underline{C}OCH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2928 (w), 1730 (m), 1701 (m), 1612 (w), 1430 (m), 1388 (m), 1278 (m), 1218 (s), 1156 (m), 1110 (w), 1042 (m), 1031 (w), 997 (m), 897 (m), 758 (m). MS (EI, 70 eV): *m/z* (%) = 656 (0.6) [M^++1], 655 (0.1) [M^+], 331 (79), 325 (14), 294 (14), 293 (21), 271 (17), 169 (100), 139 (16), 127 (46), 109 (87), 43 (56). HRMS (ESI): calcd $C_{30}H_{30}N_3O_{14}$ ([M+1]$^+$) 656.17223, found 656.17313. Anal. Calcd for $C_{30}H_{29}N_3O_{14}$: C, 54.96; H, 4.46; N, 6.41. Found: C, 55.13; H, 4.60; N, 6.28.

6-Methyl-2-phenyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39a)

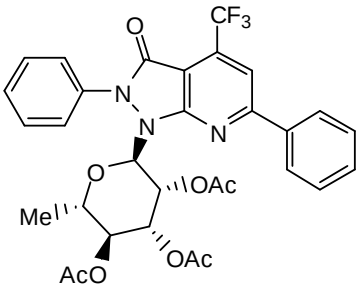


Starting from **2a** (293 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39a** was isolated as yellow foam (385 mg, 68%); mp 185-187 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (d, $^3J_{H,H}$ = 6.8 Hz, 3H, CH_3-5'), 1.97 (s, 3H, OAc-4'), 2.05 (s, 3H, OAc-3'), 2.05 (s, 3H, OAc-2'), 2.77 (s, 3H, CH_3), 3.87-3.97 (m, 1H, H-5'), 4.70 (t, $^3J_{H,H}$ = 4.1 Hz, 1H, H-4'), 5.58 (t, 1H, $^3J_{H,H}$ = 4.1 Hz, H-3'), 5.65 (d, $^3J_{H,H}$ = 8.3 Hz, 1H, H-1'), 6.86 (dd, $^3J_{H,H}$ = 8.3 Hz, $^3J_{H,H}$ = 3.6 Hz, 1H, H-2'), 7.32-7.38 (m, 2H, Ph), 7.45-7.51 (m, 2H, Ph), 7.54-7.59 (m, 2H, H-5, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.4 ($CH_{3\text{-rhamn}}$), 20.7, 20.8, 21.0 ($\underline{C}H_3CO$), 25.5 (CH_3), 67.2, 69.2, 72.4, 72.5, 81.7 (CH_{rhamn}), 105.7 (C-3a), 116.1 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^1J_{C,F}$ =

275.0 Hz, CF_3), 125.3, 127.8, 129.2 (CH_{Ar}), 135.5, (C_{Ar}), 136.5 (q, $^2J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 158.7 (C-6), 161.0 (C=O), 165.4 (C-7a), 169.1, 169.3, 169.7 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -62.73 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2934 (w), 1747 (m), 1715 (m), 1593 (w), 1486 (w), 1378 (m), 1361 (m), 1251 (m), 1218 (s), 1149 (m), 1136 (s), 1121 (m), 1049 (s), 1024 (m), 922 (m), 894 (m), 752 (m). MS (EI, 70 eV): *m/z* (%) = 565 (0.2) [M^+], 293 (21), 273 (57), 171 (21), 153 (97), 111 (87), 83 (32), 77 (29), 43 (100). HRMS (ESI): calcd $C_{26}H_{27}F_3N_3O_8$ ([M+1]$^+$) 566.17448, found 566.1747. Anal. Calcd for $C_{26}H_{26}F_3N_3O_8$: C, 55.22; H, 4.63; N, 7.43. Found: C, 55.19; H, 4.70; N, 7.30.

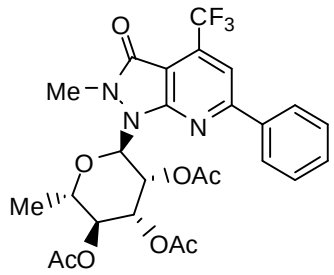
2,6-Biphenyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39b)



Starting from **2c** (355 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39b** was isolated as yellow foam (276 mg, 44%); mp 93-94 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (d, $^3J_{H,H}$ = 7.0 Hz, 3H, CH_3-5'), 1.89 (s, 3H, OAc-4'), 2.07 (s, 3H, OAc-3'), 2.08 (s, 3H, OAc-2'), 3.96-4.04 (m, 1H, H-5'), 4.72 (t, $^3J_{H,H}$ = 3.3 Hz, 1H, H-4'), 5.58 (t, 1H, $^3J_{H,H}$ = 3.3 Hz, H-3'), 5.65 (d, $^3J_{H,H}$ = 9.4 Hz, 1H, H-1'), 6.86 (dd, $^3J_{H,H}$ = 9.4 Hz, $^3J_{H,H}$ = 3.6 Hz, 1H, H-2'), 7.40 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ph), 7.52-7.69 (m, 7H, Ph), 7.98 (s, 1H, H-5), 8.26-8.29 (m, 2H, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.8 (CH_3), 20.6, 20.7, 20.8 ($\underline{C}H_3CO$), 66.7, 68.9, 71.9, 72.8, 80.2 (CH_{rhamn}), 106.8 (C-3a), 112.7 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.5 (q, $^1J_{C,F}$ = 275.0 Hz, CF_3), 124.6, 127.4, 127.8, 129.0, 129.1, 131.3 (CH_{Ar}), 135.0, 136.8 (C_{Ar}), 137.0 (q, $^2J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 158.2 (C-6), 161.1 (C=O), 161.9 (C-7a), 168.9, 169.0, 169.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.66 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3068 (w), 2943 (w), 1750 (m), 1710 (m), 1593 (m), 1489 (w), 1363 (m), 1208 (s), 1144 (m), 1032 (s) 1120 (m), 1051 (m), 1024 (s), 923 (m), 752 (m). MS (EI, 70 eV): *m/z* (%) = 628 (0.32) [M^++1], 627 (0.3) [M^+], 355 (21), 273 (90), 171 (29), 153 (96), 111 (91), 83 (25), 77 (18), 43 (100). HRMS (ESI): calcd $C_{31}H_{29}F_3N_3O_8$ ([M+1]$^+$) 628.1901, found 628.1911. Anal. Calcd for $C_{31}H_{28}F_3N_3O_8$: C, 59.33; H, 4.50; N, 6.70. Found: C, 59.48; H, 4.38; N, 6.44.

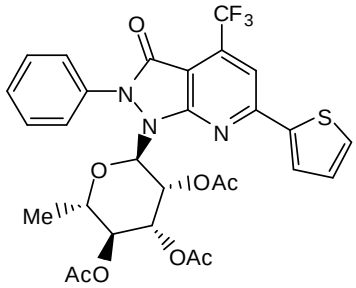
2-Methyl-6-phenyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39c)



Starting from **2d** (293 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39c** was isolated as yellow foam (322 mg, 57%); mp 81-83 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (d, $^{3}J_{H,H}$ = 7.0 Hz, 3H, CH_3-5'), 1.61 (s, 3H, OAc-4'), 1.85 (s, 3H, OAc-3'), 1.97 (s, 3H, OAc-2'), 3.41 (s, 3H, NCH_3), 4.02-4.10 (m, 1H, H-5'), 4.70 (t, $^{3}J_{H,H}$ = 3.7 Hz, 1H, H-4'), 5.45 (t, 1H, $^{3}J_{H,H}$ = 3.7 Hz, H-3'), 5.81 (d, $^{3}J_{H,H}$ = 8.5 Hz, 1H, H-1'), 6.15 (dd, $^{3}J_{H,H}$ = 8.5 Hz, $^{3}J_{H,H}$ = 3.5 Hz, 1H, H-2'), 7.33-7.37 (m, 3H, Ph), 7.66 (s, 1H, H-5), 7.93-7.96 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.1 (CH_3), 20.2, 20.7, 20.8 ($\underline{C}H_3CO$), 32.1 ($N\underline{C}H_3$), 66.7, 69.0, 71.8, 72.8, 80.3 (CH_{rhamn}), 105.6 (C-3a), 111.9 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^{1}J_{C,F}$ = 274.6 Hz, CF_3), 127.6, 129.1, 131.1 (CH_{Ar}), 136.6 (q, $^{2}J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 136.9 (C_{Ar}), 159.3 (C-6), 159.7 (C=O), 161.4 (C-7a), 168.9, 169.0, 169.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.63 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2983 (w), 2942 (w), 1747 (m), 1694 (m), 1595 (m), 1444 (w), 1410 (w), 1372 (m), 1213 (s), 1145 (s), 1050 (m), 1032 (m), 913 (m), 775 (m), 692 (m). MS (EI, 70 eV): *m/z* (%) = 565 (0.3) [M^+], 293 (34), 273 (75), 111 (94), 83 (24), 77 (54), 43 (100). HRMS (ESI): calcd $C_{26}H_{27}F_3N_3O_8$ ([M+1]$^+$) 566.17448, found 566.1746. Anal. Calcd for $C_{26}H_{26}F_3N_3O_8$: C, 55.22; H, 4.63; N, 7.43. Found: C, 55.43; H, 4.77; N, 6.97.

2-Phenyl-6-(thiophen-2-yl)-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39e)

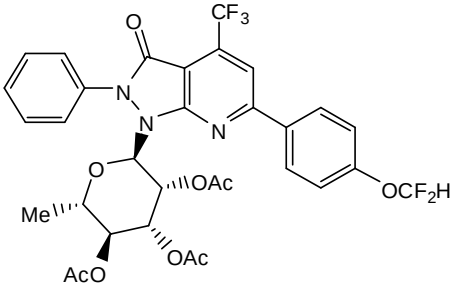


Starting from **2g** (361 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39e** was isolated as yellow foam (595 mg, 86%); mp 156-158 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (d, $^{3}J_{H,H}$ = 7.2 Hz, 3H, CH_3-5'), 1.99 (s, 3H, OAc-4'), 2.03 (s, 3H, OAc-3'), 2.04 (s, 3H, OAc-2'), 3.97-4.05 (m, 1H, H-5'), 4.69 (t, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-4'), 5.55 (t, 1H, $^{3}J_{H,H}$ = 3.3 Hz, H-3'), 5.63 (d, $^{3}J_{H,H}$ = 9.6 Hz, 1H, H-1'), 6.67 (dd, $^{3}J_{H,H}$ = 9.6 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-2'), 7.21 (dd, $^{3}J_{H,H}$ = 4.9 Hz, $^{3}J_{H,H}$ = 3.8 Hz, 1H, Hetar), 7.33-7.39 (m, 1H, Ar), 7.48-7.53 (m, 2H, Ar), 7.59-7.64 (m, 3H, Ar, Hetar), 7.77 (s, 1H, H-5), 7.90 (dd, $^{3}J_{H,H}$ = 3.8 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.1 (CH_3),

20.7, 21.0 ($\underline{C}H_3CO$), 69.2, 72.3, 73.1, 80.3 (CH_{rhamn}), 106.3 (C-3a), 111.5 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.6 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 124.8, 127.5, 128.7, 129.0, 129.2, 131.6 (CH_{Ar}), 135.2 (C_{Ar}), 136.6 (q, $^2J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 142.9, 156.9 (C_{Ar}), 158.3 (C=O), 161.1 (C-7a), 169.1, 169.2, 169.7 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.87 (s). MS (EI, 70 eV): *m/z* (%) = 634 (0.24) [M^++1], 633 (0.2) [M^+], 496 (18), 362 (32), 361 (71), 360 (21), 332 (15), 274 (39), 273 (97), 213 (56), 171 (75), 154 (25), 153 (100), 129 (25), 127 (17), 111 (99), 83 (70), 77 (62), 43 (98). HRMS (ESI): calcd $C_{29}H_{27}F_3N_3O_8S$ ([M+1]$^+$) 634.1465, found 634.1466. Anal. Calcd for $C_{29}H_{26}F_3N_3O_8S$: C, 54.97; H, 4.14; N, 6.63. Found: C, 54.71; H, 4.08; N, 6.72.

6-(4-(Difluoromethoxy)phenyl)-2-phenyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39g)

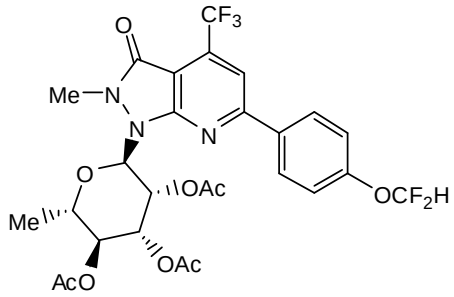


Starting from **2r** (421 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39g** was isolated as yellow foam (423 mg, 61%); mp 93-94 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (d, $^3J_{H,H}$ = 7.0 Hz, 3H, CH_3), 1.87 (s, 3H, OAc-4'), 2.04 (s, 3H, OAc-3'), 2.06 (s, 3H, OAc-2'), 3.92-4.00 (m, 1H, H-5'), 4.70 (t, $^3J_{H,H}$ = 3.3 Hz, 1H, H-3'), 5.55 (t, $^3J_{H,H}$ = 3.3 Hz, 1H, H-4'), 5.59 (d, $^3J_{H,H}$ = 9.4 Hz, 1H, H-1'), 6.63 (t, $^2J_{F,H}$ = 73.1 Hz, 1H, OCF_2H), 6.84 (dd, $^3J_{H,H}$ = 9.4 Hz, $^3J_{H,H}$ = 3.3 Hz, 1H, H-2'), 7.30-7.33 (m, 2H, Ar), 7.35-7.40 (m, 1H, Ar), 7.49-7.54 (m, 2H, Ar), 7.62-7.65 (m, 2H, Ar), 7.91 (1H, s, H-5), 8.25-8.30 (2H, m, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.9 (CH_3), 20.7, 20.7, 20.8 ($\underline{C}H_3CO$), 66.8, 69.0, 72.0, 73.1, 80.2 (CH_{rhamn}), 107.2 (C-3a), 112.5 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 115.6 (t, $^1J_{C,F}$ = 261.3 Hz, OCF_2H), 119.9 (CH_{Ar}), 121.6 (q, $^1J_{C,F}$ = 275.2 Hz, CF_3), 124.8, 127.6, 129.3, 129.7 (CH_{Ar}), 134.0, 135.1 (C_{Ar}), 137.4 (q, $^2J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 153.6 (t, $^3J_{C,F}$ = 2.8 Hz, $\underline{C}OCF_2H$), 158.2 (C-6), 160.7 (C=O), 161.2 (C-7a), 169.2, 169.2, 169.5 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -81.64 (d, $^2J_{H,F}$ = 12.3 Hz, 2F, OCF_2H), -62.66 (s, 3F, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2944 (w), 2640 (w), 1749 (m), 1704 (m), 1593 (m), 1372 (m), 1212 (s), 1146 (m), 1118 (m), 1042 (s), 912 (w), 841 (w).

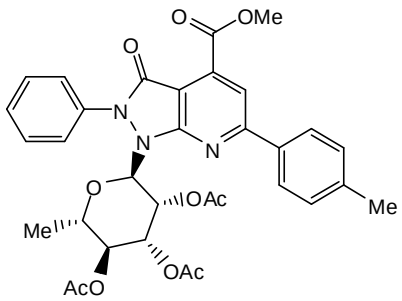
MS (EI, 70 eV): *m/z* (%) = 694 (0.12) [M^+], 421 (32), 273 (76), 171 (31), 153 (91), 111 (91), 83 (28), 77 (32), 43 (100). HRMS (ESI): calcd $C_{32}H_{29}F_5N_3O_9$ ([M+1]$^+$) 694.1818, found 694.1829. Anal. Calcd for $C_{32}H_{28}F_5N_3O_9$: C, 55.41; H, 4.07; N, 6.06. Found: C, 55.46; H, 4,06; N, 5.90.

6-(4-(Difluoromethoxy)phenyl)-2-methyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (39h)



Starting from **2s** (359 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39h** was isolated as yellow foam (404 mg, 64%); mp 190-192 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, $^{3}J_{H,H}$ = 7.0 Hz, 3H, CH_3), 1.84 (s, 3H, OAc-4'), 2.03 (s, 3H, OAc-3'), 2.16 (s, 3H, OAc-2'), 3.60 (s, 3H, NCH_3), 4.19-4.27 (m, 1H, H-5'), 4.89 (t, $^{3}J_{H,H}$ = 3.7 Hz, 1H, H-3'), 5.64 (t, $^{3}J_{H,H}$ = 3.7 Hz, 1H, H-4'), 5.93 (d, $^{3}J_{H,H}$ = 8.5 Hz, 1H, H-1'), 6.42 (dd, $^{3}J_{H,H}$ = 8.5 Hz, $^{3}J_{H,H}$ = 3.7 Hz, 1H, H-2'), 6.61 (t, $^{2}J_{F,H}$ = 73.1 Hz, 1H, OCF_2H), 7.27-7.30 (m, 2H, Ar), 7.80 (1H, s, H-5), 8.13-8.18 (2H, m, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.3 (CH_3), 20.5, 20.9, 20.9 ($\underline{C}H_3CO$), 32.1 (NCH_3), 66.8, 69.1, 72.0, 72.8, 80.5 (CH_{rhamn}), 106.1 (C-3a), 111.8 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 115.6 (t, $^{1}J_{C,F}$ = 261.3 Hz, OCF_2H), 119.9 (CH_{Ar}), 121.8 (q, $^{1}J_{C,F}$ = 275.2 Hz, CF_3), 129.5 (CH_{Ar}), 134.1 (C_{Ar}), 136.9 (q, $^{2}J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 153.4 (t, $^{3}J_{C,F}$ = 2.8 Hz, $\underline{C}OCF_2H$), 159.3 (C-6), 159.8 (C=O), 160.3 (C-7a), 169.2, 169.2, 169.7 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, CDCl3): δ = -81.56 (2F, s, OCF_2H), -62.65 (3F, s, CF_3). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2947 (w), 1748 (m), 1694 (m), 1597 (m), 1373 (m), 1216 (s), 1124 (m), 1049 (s), 915 (w), 841 (m). MS (EI, 70 eV): *m/z* (%) = 631 (0.1) [M^+], 359 (25), 273 (80), 213 (13), 171 (27), 153 (100), 111 (93), 83 (31), 43 (87). HRMS (ESI): calcd $C_{27}H_{27}F_5N_3O_9$ ([M+1]$^+$) 632.1662, found 632.16622. Anal. Calcd for $C_{27}H_{26}F_5N_3O_9$: C, 51.35; H, 4.15; N, 6.65. Found: C, 51.54; H, 4.29; N, 6.86.

Methyl 3-oxo-2-phenyl-6-*p*-tolyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (39i)

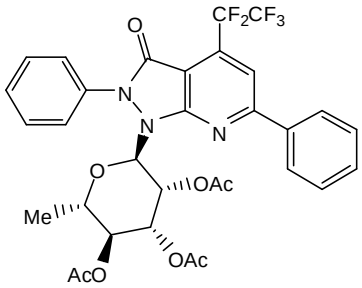


Starting from **2u** (359 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39i** was isolated as yellow foam (373 mg, 59%); mp 98-100 ^{o}C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (d, $^{3}J_{H,H}$ = 6.8 Hz, 3H, 5'-CH_3), 1.92 (s, 3H, OAc-4'), 2.02 (s, 3H, OAc-3'), 2.04 (s, 3H, OAc-2'), 2.44 (s, 3H, Ar-CH_3), 3.92-3.99 (m, 1H, H-5'), 4.04 (s, 3H, CO_2CH_3), 4.69 (t, $^{3}J_{H,H}$ = 3.6 Hz, 1H, H-3'), 5.55 (t, $^{3}J_{H,H}$ = 3.6 Hz, 1H, H-4'), 5.62 (d, $^{3}J_{H,H}$ = 9.2 Hz, 1H, H-1'), 6.76 (dd, $^{3}J_{H,H}$ = 9.2 Hz, $^{3}J_{H,H}$ = 3.6 Hz, 1H, H-2'), 7.33-7.38 (m, 3H, Ar), 7.47-7.52 (m, 2H, Ar), 7.60-7.64 (m, 2H, Ar), 7.98 (s, 1H, H-5), 8.12-8.15 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 16.3 (CH_3), 20.8, 20.8, 20.8 ($\underline{C}H_3CO$), 21.6

(CH_{3rhamn}), 53.3 (OCH_3), 67.0, 69.3, 72.4, 72.6, 81.0 (CH_{rhamn}), 107.7 (C-3a), 115.9 (C-5), 125.0, 127.4, 127.8, 129.2, 129.9 (CH_{Ar}), 134.5, 135.8, 139.4, 141.6, 159.6 (C_{Ar}), 161.2 (C=O), 161.5 (C-7a), 165.6 ($\underline{C}O_2CH_3$), 169.2, 169.3, 169.7 ($CH_3\underline{C}O$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2923 (w), 2852 (w), 1740 (s), 1703 (m), 1583 (m), 1364 (m), 1210 (s), 1048 (s), 947 (m), 912 (m), 825 (m), 734 (m). HRMS (ESI): calcd $C_{33}H_{34}N_3O_{10}$ ($[M+1]^+$) 632.2239, found 632.2238. Anal. Calcd for $C_{33}H_{33}N_3O_{10}$: C, 62.75; H, 5.27; N, 6.65. Found: C, 62.80; H, 5.19; N, 6.47.

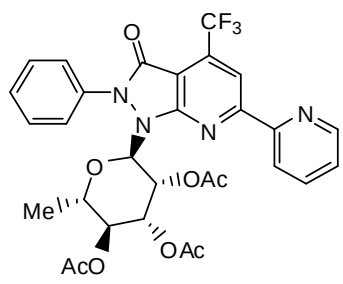
4-(Perfluoroethyl)-2,6-phenyl-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (39j)



Starting from **2v** (405 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39j** was isolated as yellow foam (576 mg, 85%); mp 172-174 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16 (d, $^3J_{H,H}$ = 7.1 Hz, 3H, CH_3), 1.86 (s, 3H, OAc-4'), 2.04 (s, 3H, OAc-3'), 2.04 (s, 3H, OAc-2'), 3.94-3.99 (m, 1H, H-5'), 4.69 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, H-3'), 5.54 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, H-4'), 5.65 (d, $^3J_{H,H}$ = 9.5 Hz, 1H, H-1'), 6.81 (dd, $^3J_{H,H}$ = 9.5 Hz, $^3J_{H,H}$ = 3.4 Hz, 1H, H-2'), 7.34-7.40 (m, 1H, Ar), 7.48-7.66 (m, 7H, Ar), 7.91 (s, 1H, H-5), 8.23-8.27 (m, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4, 20.5, 20.7 ($\underline{C}H_3CO$), 62.8 (CH_2), 69.5, 71.6, 78.7, 92.8 (CH_{rib}), 111.4 (C-3a), 118.8 (t, $^3J_{C,F}$ = 7.8 Hz, C-5), 124.8, 125.4, 127.8, 128.2, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 137.1, 149.6 (CH_{Ar}), 139.2 (t, $^2J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 150.5, 150.8 (C_{Ar}), 159.4 (C=O), 160.0 (C-7a), 169.3, 169.3, 170.5 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -111.7 0 (s, 2F, CF_2), -83.17 (s, 3F, CF_3). MS (EI, 70 eV): *m/z* (%) = 677 (0.2) [M^+], 405 (88), 376 (23), 273 (82), 171 (35), 153 (100), 111 (89), 83 (34), 77 (22), 43 (48). HRMS (ESI): calcd $C_{32}H_{29}F_5N_3O_8$ ($[M+1]^+$) 678.1846, found 678.1849.Anal. Calcd for $C_{32}H_{28}F_5N_3O_8$: C, 56.72; H, 4.17; N, 6.20. Found: C, 56.59; H, 4.19; N, 6.17.

2-Phenyl-6-(pyridin-2-yl)-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-4-(Trifluoromethyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (39l)

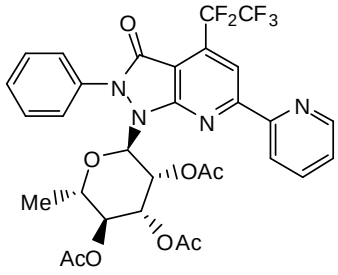


Starting from **2x** (356 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39l** was isolated as yellow foam (528 mg, 84%); mp 68-69 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (d, $^3J_{H,H}$ = 6.9 Hz, 3H, CH_3), 1.93 (s, 3H, OAc-4'), 2.05 (s, 3H, OAc-3'), 2.05 (s, 3H, OAc-2'), 3.94-4.03 (m, 1H, H-5'), 4.68 (t, $^3J_{H,H}$ = 3.4 Hz, 1H, H-

3'), 5.51 (t, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-4'), 5.78 (d, $^{3}J_{H,H}$ = 9.3 Hz, 1H, H-1'), 6.21 (dd, $^{3}J_{H,H}$ = 9.5 Hz, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-2'), 7.37-7.62 (m, 6H, Ar), 7.86 (td, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, Ar), 8.28 (s, 1H, H-5), 8.53 (dt, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Ar), 8.79-8.81 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.8 (CH_3), 20.6, 20.7, 20.8 ($\underline{C}H_3CO$), 66.7, 68.9, 71.9, 72.8, 80.2 (CH_{rhamn}), 106.8 (C-3a), 112.7 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.5 (q, $^{1}J_{C,F}$ = 275.0 Hz, CF_3), 124.6, 127.4, 127.8, 129.0, 129.1, 131.3 (CH_{Ar}), 135.0, 136.8 (C_{Ar}), 137.0 (q, $^{2}J_{C,F}$ = 36.3 Hz, $\underline{C}CF_3$), 153.6 (t, $^{3}J_{C,F}$ = 2.8 Hz, $\underline{C}OCF_2H$), 158.2 (C-6), 161.1 (C=O), 161.9 (C-7a), 168.9, 169.0, 169.4 ($CH_3\underline{C}O$). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -67.79 (s). MS (EI, 70 eV): *m/z* (%) = 629 (0.21) [M+1], 628 (0.4) [M^+], 356 (33), 273 (57), 213 (13), 171 (21), 153 (100), 111 (90), 83 (23), 77 (12), 43 (89). HRMS (ESI): calcd $C_{30}H_{28}F_3N_4O_8$ ([M+1]$^+$) 629.18537, found 629.18622. Anal. Calcd for $C_{30}H_{27}F_3N_4O_8$: C, 57.33; H, 4.33; N, 8.91. Found: C, 57.12; H, 4.30; N, 8.95.

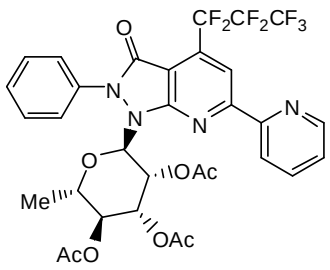
4-(Perfluoroethyl)-2-phenyl-6-(pyridin-2-yl)-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (39m)



Starting from **2y** (406 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39m** was isolated as yellow foam (563 mg, 83%); mp 72-74 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (d, $^{3}J_{H,H}$ = 6.9 Hz, 3H, CH_3), 1.88 (s, 3H, OAc-4'), 2.03 (s, 3H, OAc-3'), 2.04 (s, 3H, OAc-2'), 3.97 (dq, $^{3}J_{H,H}$ = 6.9 Hz, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-5'), 4.66 (t, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-3'), 5.47 (t, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-4'), 5.83 (d, $^{3}J_{H,H}$ = 9.5 Hz, 1H, H-1'), 6.15 (dd, $^{3}J_{H,H}$ = 9.5 Hz, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-2'), 7.36-7.46 (m, 2H, Ar), 7.49-7.55 (m, 2H, Ar), 7.58-7.63 (m, 2H, Ar), 7.85 (td, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 1.7 Hz, 1H, Ar), 8.31 (s, 1H, H-5), 8.53 (dt, $^{3}J_{H,H}$ = 7.9 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Ar), 8.79-8.82 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 15.8 (CH_3), 20.6, 20.7, 20.8 ($\underline{C}H_3CO$), 66.7, 68.9, 71.9, 72.8, 80.2 (CH_{rhamn}), 111.5 (C-3a), 118.5 (C-5), 125.2, 125.3, 127.6, 128.1, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 136.6 (CH_{Ar}), 139.2 (t, $^{2}J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 150.1 (CH_{Ar}), 150.4, 151.1 (C_{Ar}), 159.4 (C=O), 160.0 (C-7a), 168.9, 169.0, 169.4 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -82.67 (s, 3F, CF_3), -116.48 (q, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 678 (0.5) [M^+], 407 (15), 406 (35), 273 (68), 213 (15), 171 (22), 153 (100), 111 (55), 57 (20), 43 (51), 41 (17). HRMS (ESI): calcd $C_{31}H_{28}F_5N_4O_8$ ([M+1]$^+$) 679.18218, found 679.18303. Anal. Calcd for $C_{31}H_{27}F_5N_4O_8$: C, 54.87; H, 4.01; N, 8.26. Found: C, 54.60; H, 3.99; N, 8.28.

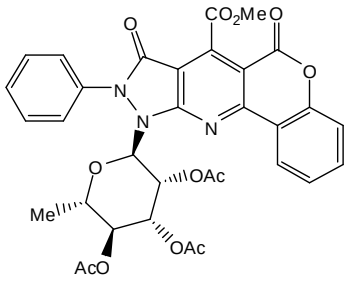
4-(Perfluoropropyl)-2-phenyl-6-(pyridin-2-yl)-1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (39n)



Starting from **2z** (456 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39n** was isolated as yellow foam (612 mg, 84%); mp 76-78 ^{o}C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19 (d, $^{3}J_{H,H}$ = 6.9 Hz, 3H, CH_3), 1.85 (s, 3H, OAc-4'), 2.01 (s, 3H, OAc-3'), 2.04 (s, 3H, OAc-2'), 3.91-4.01 (m, 1H, H-5'), 4.66 (t, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-3'), 5.46 (t, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-4'), 5.87 (d, $^{3}J_{H,H}$ = 9.5 Hz, 1H, H-1'), 6.10 (dd, $^{3}J_{H,H}$ = 9.5 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-2'), 7.36-7.46 (m, 2H, Ar), 7.49-7.55 (m, 2H, Ar), 7.59-7.63 (m, 2H, Ar), 7.85 (td, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.8 Hz, 1H, Ar), 8.29 (s, 1H, H-5), 8.55 (dt, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Ar), 8.79-8.82 (m, 1H, Ar). ^{13}C NMR (62.8 MHz, $CDCl_3$): δ = 15.8 (CH_3), 20.6, 20.7, 20.8 ($\underline{C}H_3CO$), 66.7, 68.9, 71.9, 72.8, 80.2 (CH_{rhamn}), 111.4 (C-3a), 118.8 (t, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 124.8, 125.4, 127.8, 128.2, 129.4 (CH_{Ar}), 134.9 (C_{Ar}), 137.1, 149.6 (CH_{Ar}), 139.2 (t, $^{2}J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 150.5, 150.8 (C_{Ar}), 159.4 (C=O), 160.0 (C-7a), 168.9, 169.0, 169.4 ($CH_3\underline{C}O$). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -80.02 (t, $^{3}J_{F,F}$ = 9.7 Hz, 3F, CF_3), -112.64 (dq, $^{2}J_{F,F}$ = 275.0 Hz, $^{3}J_{F,F}$ = 9.7 Hz, 1F, CF_3), -115.27 (dq, $^{2}J_{F,F}$ = 275 Hz, $^{3}J_{F,F}$ = 9.7 Hz, 1F, CF_3), -125.50 (s, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 728 (0.8) [M^+], 456 (41), 273 (82), 171 (22), 153 (100), 111 (88), 83 (24), 77 (13), 43 (94). HRMS (ESI): calcd $C_{32}H_{28}F_7N_4O_8$ ([M+1]$^+$) 729.17899, found 729.17998. Anal. Calcd for $C_{32}H_{27}F_7N_4O_8$: C, 52.75; H, 3.74; N, 7.69. Found: C, 52.52; H, 3.72; N, 7.72.

Methyl 1-(2,3,4-tri-O-acetyl-α-L-rhamnopyranozyl)-6,8-dioxo-9-phenyl-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylate (39v)



Starting from **22c** (387 mg, 1 mmol) and 1,2,3,4-tetra-O-acetyl-α-L-rhamnose (332 mg, 1mmol), **39v** was isolated as yellow foam (442 mg, 67%); mp 138-140 ^{o}C.

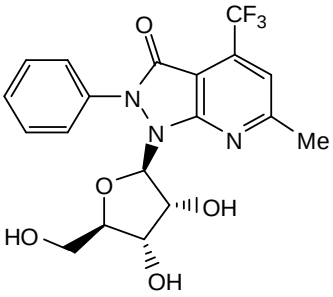
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, $^{3}J_{H,H}$ = 7.1 Hz, 3H, 5'-CH_3), 1.99 (s, 3H, OAc-4'), 2.05 (s, 3H, OAc-3'), 2.07 (s, 3H, OAc-2'), 3.96-4.04 (m, 1H, H-5'), 4.11 (s, 3H, CO_2CH_3), 4.72 (t, $^{3}J_{H,H}$ = 3.2 Hz, 1H, H-3'), 5.59 (t, $^{3}J_{H,H}$ = 3.2 Hz, 1H, H-4'), 5.65 (d, $^{3}J_{H,H}$ = 9.6 Hz, 1H, H-1'), 6.85-6.87 (m, 1H, H-2'), 7.37-7.71 (m, 8H, Ar), 8.67-8.71 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.8, 20.8, 20.8 ($\underline{C}H_3CO$), 21.6 (CH_{3rhamn}), 53.3 (OCH_3), 67.0, 69.3, 72.4, 72.6, 81.0 (CH_{rhamn}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9

(CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a), 167.9 ($\underline{C}O_2CH_3$), 169.2, 169.3, 169.7 ($CH_3\underline{C}O$). HRMS (ESI): calcd $C_{33}H_{30}N_3O_{12}$ ($[M+1]^+$) 660.1824, found 660.18265. Anal. Anal. Calcd for $C_{33}H_{29}N_3O_{12}$: C, 60.09; H, 4.43; N, 6.37. Found: C, 60.35; H, 4.72; N, 6.19.

A.2.7. General procedure for synthesis of compounds 40-42

Acetylated nucleoside **37-39** (0.5 mmol) was dissolved in 20mL MeOH and 5 mL of ammonia (7N solution in MeOH) was added. The mixture was stirred at room temperature overnight and, if necessary, for up to 24h more (controlled by TLC). Afterwards, the solution was evaporated under reduced pressure and crystallized from CH_2Cl_2/MeOH, or subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

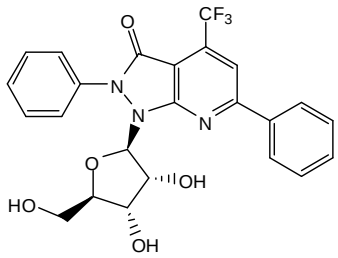
6-Methyl-2-phenyl-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40a)



Starting from **37a** (276 mg, 1 mmol), **40a** was isolated via column chromatography as yellow solid (204 mg, 96%); mp 98-100 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.74 (s, 3H, CH_3), 3.01-3.06 (m, 1H, H_a-5'), 3.15-3.20 (m, 1H, H_b-5'), 3.60-3.65 (m, 1H, H-4'), 3.86 (dd, $^2J_{H,H}$ = 8.9 Hz, $^3J_{H,H}$ = 5.1 Hz, 1H, H-3'), 4.56 (t, $^3J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 4.83 (dd, $^2J_{H,H}$ = 11.6 Hz, $^3J_{H,H}$ = 5.9 Hz, 1H, H-2'), 5.04 (d, $^3J_{H,H}$ = 5.1 Hz, 1H, OH-3'), 5.35 (d, $^3J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.48 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, H-1'), 7.38-7.46 (m, 1H, Ph), 7.52-7.59 (m, 4H, Ph), 7.67 (s, 1H, H-5). ^{13}C NMR (62.9 MHz, DMSO-d6): δ = 24.8 (CH_3), 61.3 (CH_2), 69.8, 70.7, 84.6, 93.7 (CH_{rib}), 104.3 (C-8), 116.0 (q, $^3J_{C,F}$ = 5.6 Hz, C-5), 121.6 (q, $^1J_{C,F}$ = 274.4 Hz, CF_3), 124.8, 127.2, 128.9 (CH_{Ar}), 134.1 (q, $^2J_{C,F}$ = 35.6 Hz, $\underline{C}CF_3$), 135.4 (C_{Ar}), 158.0 (C-6), 160.5 (CO), 165.6 (C-9). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.33 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3369 (br w), 3066 (w), 2929 (w), 1679 (m), 1592 (m), 1488 (w), 1362 (m), 1144 (s), 1035 (m). MS (EI, 70 eV): *m/z* (%) = 425 (0.12) [M^+], 293 (25), 259 (76), 139 (100), 97 (68), 77 (28), 43 (60). HRMS (ESI): calcd $C_{19}H_{19}F_3N_3O_5$ ($[M+1]^+$) 426.1271, found 426.1273. Anal. Calcd for $C_{19}H_{18}F_3N_3O_5$: C, 53.65; H, 4.27; N, 9.88. Found: C, 53.59; H, 4.23; N, 9.46.

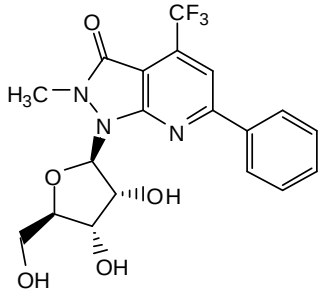
2,6-Biphenyl-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40b)



Starting from **37b** (307 mg, 0.5 mmol), **40b** was isolated via crystallization (CH_2Cl_2/MeOH) as colorless solid (224 mg, 92%); mp 215-217 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.97-3.02 (m, 1H, H_a-5'), 3.11-3.16 (m, 1H, H_b-5'), 3.64 (q, $^3J_{H,H}$ = 5.0 Hz, 1H, H-4'), 3.91 (q, $^3J_{H,H}$ = 5.0 Hz, 1H, H-3'), 4.53 (t, $^3J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 5.04 (q, $^3J_{H,H}$ = 5.9 Hz, 1H, H-2'), 5.11 (d, $^3J_{H,H}$ = 5.3 Hz, 1H, OH-3'), 5.45 (d, $^3J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.57 (d, $^3J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.41-7.47 (m, 1H, Ph), 7.56-7.65 (m, 7H, Ph), 8.25 (s, 1H, H-5), 8.32-8.35 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.1 (CH_2), 69.7, 70.8, 84.4, 93.9 (CH_{rib}), 105.7 (C-3a), 112.7 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.7 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 124.9, 127.3, 127.8, 129.0, 129.2, 131.4 (CH_{Ar}), 135.0 (q, $^2J_{C,F}$ = 35.9 Hz, $\underline{C}CF_3$), 135.3, 136.2, 157.8 (C_{Ar}), 160.7 (C=O), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.10 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3375 (br w), 2958 (w), 1677 (s), 1593 (m), 1377 (m), 1269 (m), 1174 (m), 1139 (m), 1093 (s), 1037 (m), 1018 (m), 983 (m), 887 (m), 754 (m), 690 (m), 666 (m). MS (EI, 70 eV): *m/z* (%) = 487 (0.13) [M^+], 355 (40), 259 (99), 139 (100), 97 (74), 77 (49), 43 (93). HRMS (ESI): calcd $C_{24}H_{21}F_3N_3O_5$ ([M+1]$^+$) 488.14278, found 488.14286. Anal. Calcd for $C_{24}H_{20}F_3N_3O_5$: C, 59.14; H, 4.14; N, 8.62. Found: C, 60.04; H, 4.09; N, 8.37.

2-Methyl-6-phenyl-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40c)

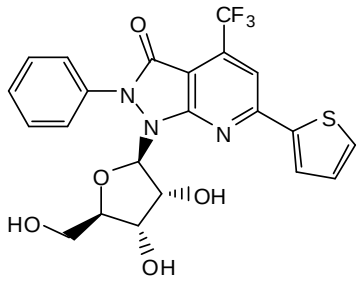


Starting from **37c** (276 mg, 0.5 mmol), **40c** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (203 mg, 95%); mp 226-228 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.41-3.46 (m, 1H, H_a-5'), 3.52 (s, 3H, CH_3), 3.54-3.58 (m, 1H, H_b-5'), 3.84 (q, $^3J_{H,H}$ = 3.9 Hz, 1H, H-4'), 4.03-4.08 (m, 1H, H-3'), 4.64 (q, $^3J_{H,H}$ = 6.4 Hz, 1H, H-2'), 4.84 (t, $^3J_{H,H}$ = 5.3 Hz, 1H, OH-5'), 5.16 (d, $^3J_{H,H}$ = 5.0 Hz, 1H, OH-3'), 5.27 (d, $^3J_{H,H}$ = 6.4 Hz, 1H, OH-2'), 6.00 (d, $^3J_{H,H}$ = 6.4 Hz, 1H, H-1'), 7.56-7.58 (m, 3H, Ph), 8.04 (s, 1H, H-5), 8.22-8.25 (m, 2H, Ph). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 32.0 (CH_3), 61.2 (CH_2), 69.5, 70.6, 84.5, 92.2 (CH_{rib}), 104.5 (C-3a), 111.4 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 120.1 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 127.7, 129.1, 131.0 (CH_{Ar}), 134.7 (q, $^2J_{C,F}$ = 35.6 Hz, $\underline{C}CF_3$), 136.5, 158.6 (C_{Ar}), 158.7 (C=O), 160.5 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.03 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3334 (br w), 3075 (w), 2929 (w), 1694 (s), 1594 (m), 1371 (m), 1263 (m), 1227

(m), 1150 (m), 1103 (s), 1044 (s), 992 (m), 879 (m), 754 (m), 691 (m), 654 (s). MS (EI, 70 eV): *m/z* (%) = 425 (0.14) [M^+], 293 (34), 259 (90), 139 (100), 97 (45), 77 (19), 43 (39). HRMS (ESI): calcd $C_{19}H_{19}F_3N_3O_5$ ([M+1]$^+$) 426.12713, found 426.1278. Anal. Calcd for $C_{19}H_{18}F_3N_3O_5$: C, 53.65; H, 4.27; N, 9.88. found: C, 53.69; H, 4.32; N, 9.64.

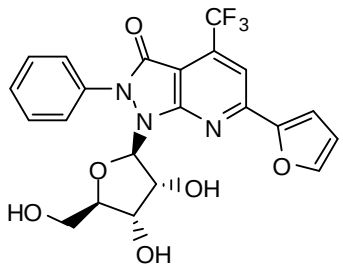
2-Phenyl-1-β-D-ribofuranozyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40e)



Starting from **37e** (310 mg, 0.5 mmol), **40e** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (220 mg, 89%); mp 227-229 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.99-3.04 (m, 1H, H_a-5'), 3.21-3.26 (m, 1H, H_b-5'), 3.62 (dd, $^3J_{H,H}$ = 9.9 Hz, $^3J_{H,H}$ = 5.8 Hz, 1H, H-4'), 3.96 (dd, $^3J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 5.2 Hz, 1H, H-3'), 4.53 (t, $^3J_{H,H}$ = 5.6 Hz, 1H, OH-5'), 5.05-5.12 (m, 2H, H-2', OH-3'), 5.36 (d, $^3J_{H,H}$ = 5.9 Hz, 1H, OH-2'), 5.48 (d, $^3J_{H,H}$ = 5.9 Hz, 1H, H-1'), 7.31 (dd, $^3J_{H,H}$ = 4.9 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, Hetar), 7.38-7.44 (m, 1H, Ar), 7.53-7.60 (m, 4H, Ar), 7.96 (dd, $^3J_{H,H}$ = 5.0 Hz, $^4J_{H,H}$ = 0.9 Hz, 1H, Hetar), 8.22 (s, 1H, H-5), 7.93 (dd, $^3J_{H,H}$ = 3.8 Hz, $^4J_{H,H}$ = 0.9 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.3 (CH_2), 69.8, 70.9, 84.6, 93.9 (CH_{rib}), 105.0 (C-3a), 111.4 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.7 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 124.7, 127.2, 129.1, 129.3, 130.4, 132.6 (CH_{Ar}), 135.0 (C_{Ar}), 135.2 (q, $^2J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 142.1, 156.4 (C_{Ar}), 157.6 (C=O), 160.3 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.21 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3411 (br w), 2958 (w), 1674 (s), 1594 (m), 1538 (m), 1495 (w), 1427 (m), 1393 (m), 1379 (m), 1367 (m), 1269 (m), 1139 (m), 1103 (m), 1090 (m), 1038 (m), 981 (m), 887 (m), 849 (m), 755 (m), 708 (s). MS (EI, 70 eV): *m/z* (%) = 493 (0.2) [M^+], 362 (36), 361 (100), 341 (15), 332 (37), 77 (31). HRMS (ESI): calcd $C_{22}H_{19}F_3N_3O_5S$ ([M+1]$^+$) 494.0992, found 494.0993. Anal. Calcd for $C_{22}H_{18}F_3N_3O_5S$: C, 53.55; H, 3.68; N, 8.52. Found: C, 53.74; H, 3.69; N, 8.47.

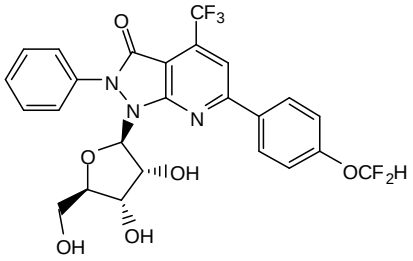
6-(Furan-2-yl)-2-phenyl-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40f)



Starting from **37f** (302 mg, 0.5 mmol), **40f** was isolated via column chromatography as yellow solid (223 mg, 93%); mp 207-209 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.98-3.06 (m, 1H, H_a-5'), 3.17-3.25 (m, 1H, H_b-5'), 3.61-3.66 (m, 1H, H-4'), 3.96 (dd, $^{3}J_{H,H}$ = 9.1 Hz, $^{3}J_{H,H}$ = 5.1 Hz, 1H, H-3'), 4.52 (t, $^{3}J_{H,H}$ = 5.9 Hz, 1H, OH-5'), 4.98-5.04 (m, 1H, H-2'), 5.09 (d, $^{3}J_{H,H}$ = 5.1 Hz, 1H, OH-3'), 5.41 (d, $^{3}J_{H,H}$ = 5.9 Hz, 1H, OH-2'), 5.46 (d, $^{3}J_{H,H}$ = 5.9 Hz, 1H, H-1'), 6.86 (dd, $^{3}J_{H,H}$ = 3.5 Hz, $^{4}J_{H,H}$ = 1.8 Hz, 1H, Hetar), 7.40-7.45 (m, 1H, Ar), 7.54-7.61 (m, 4H, Ar), 7.64 (dd, $^{3}J_{H,H}$ = 3.5 Hz, $^{4}J_{H,H}$ = 0.8 Hz, 1H, Hetar), 7.96 (s, 1H, H-5), 8.10 (dd, $^{4}J_{H,H}$ = 1.8 Hz, $^{4}J_{H,H}$ = 0.8 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.2 (CH_2), 69.8, 70.9, 84.6, 93.8 (CH_{rib}), 104.9 (C-8), 110.8 (C-5), 121.6 (q, $^{1}J_{C,F}$ = 274.4 Hz, CF_3), 113.4, 114.5, 124.7, 127.2, 129.0, 135.2 (CH_{Ar}), 135.2 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 135.2, 147.2, 151.1, 152.2 (C_{Ar}), 157.6 (CO), 160.5 (C-9). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.48 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3453 (br w), 2926 (w), 1668 (m), 1652 (m), 1603 (m), 1571 (m), 1425 (w), 1365 (s), 1296 (w), 1266 (m), 1146 (s), 1041 (s), 1015 (s), 880 (m). MS (EI, 70 eV): *m/z* (%) = 477 (0.1) [M^+], 345 (100), 316 (26), 77(19). HRMS (ESI): calcd $C_{22}H_{19}F_3N_3O_6$ ([M+1]$^+$) 478.12205, found 478.12215. Anal. Calcd for $C_{22}H_{18}F_3N_3O_6$: C, 55.35; H, 3.80; N, 8.80. Found: C, 55.62; H, 4.00; N, 8.62.

6-(4-(Difluoromethoxy)phenyl)-2-phenyl-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40g)

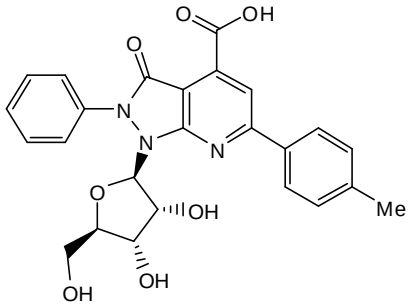


Starting from **37g** (340 mg, 0.5 mmol), **40g** was isolated via crystallization (CH_2Cl_2/MeOH) as colorless solid (271 mg, 98%); mp 185-187 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.93-3.00 (m, 1H, H_a-5'), 3.06-3.14 (1H, m, H_b-5'), 3.61 (q, $^{3}J_{H,H}$ = 5.2 Hz, 1H, H-4'), 3.88 (q, $^{3}J_{H,H}$ = 5.2 Hz, 1H, H-3'), 4.50 (t, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 4.99 (q, $^{3}J_{H,H}$ = 6.0 Hz, 1H, H-2'), 5.08 (d, $^{3}J_{H,H}$ = 5.2 Hz, 1H, OH-3'), 5.41 (d, $^{3}J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.52 (d, $^{3}J_{H,H}$ = 6.0 Hz, H-1'), 7.38-7.41 (m, 3H, Ar), 7.43 (t, $^{2}J_{F,H}$ = 73.6 Hz, 1H, OCF_2H), 7.53-7.61 (m, 4H, Ar), 8.24 (s, 1H, H-5), 8.38-8.41 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.1 (CH_2), 96.7, 70.8, 84.4, 94.0 (CH_{rib}), 105.7 (C-3a), 112.7 (q, $^{3}J_{C,F}$ = 5.5 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.0 Hz, OCF_2H), 118.8 (CH_{Ar}), 121.7 (q, $^{1}J_{C,F}$ = 275.1 Hz, CF_3), 124.9, 127.3, 129.0, 129.9 (CH_{Ar}), 133.0, 135.3 (C_{Ar}), 135.4 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 153.4

(t, $^{3}J_{C,F}$ = 3.2 Hz, <u>C</u>OCF$_2$H), 157.8 (C-6), 160.2 (C=O), 160.6 (C-7a). ^{19}F NMR (282 MHz, DMSO-d$_6$): δ = -61.09 (s, 3F, CF$_3$), -82.85 (s, 2F, OCF$_2$H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3334 (br w), 3075 (w), 2929 (w), 1694 (s), 1594 (m), 1371 (m), 1263 (m), 1227 (m), 1150 (m), 1103 (s), 1044 (s), 1009 (s), 844 (m), 729 (m), 669 (m). MS (EI, 70 eV): *m/z* (%) = 553 (0.03) [M$^+$], 421 (100), 362 (22), 77 (27). HRMS (ESI): calcd $C_{25}H_{21}F_5N_3O_6$ ([M+1]$^+$) 554.1345, found 554.1347. Anal. Calcd for $C_{25}H_{20}F_5N_3O_6$: C, 54.26; H, 3.64; N, 7.59. Found: C, 54.107; H, 3.646; N, 7.239.

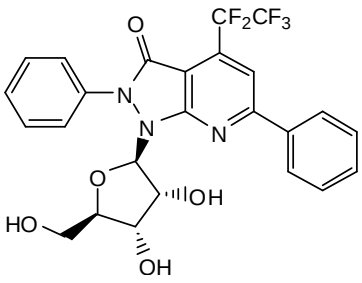
3-Oxo-2-phenyl-1-β-D-ribofuranozyl-6-*p*-tolyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (40i)



Starting from **37i** (309 mg, 0.5 mmol), **40i** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (213 mg, 89%); mp 267-268 °C.

^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.41 (s, 3H, CH$_3$), 2.89-2.97 (m, 1H, H$_a$-5'), 3.07-3.14 (m, 1H, H$_a$-5'), 3.59 (q, $^{3}J_{H,H}$ = 4.9 Hz, 1H, H-4'), 3.87 (q, $^{3}J_{H,H}$ = 4.9 Hz, 1H, H-3'), 4.49 (t, $^{3}J_{H,H}$ = 4.9 Hz, 1H, OH-5'), 5.02-5.08 (m, 2H, H-2', OH-3'), 5.42 (d, $^{3}J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.51 (d, $^{3}J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.40-7.43 (m, 2H, Ar), 7.46-7.49 (m, 1H, Ar), 7.56-7.64 (m, 4H, Ar), 8.12-8.15 (m, 2H, Ar), 8.37 (s, 1H, H-5), 11.93 (s, 1H, CO$_2$H). ^{13}C NMR (62.9 MHz, DMSO-d$_6$): δ = 20.9 (CH$_3$), 61.2 (CH$_2$), 69.7, 70.8, 84.3, 94.0 (CH$_{rib}$), 106.2 (C-3a), 116.2, 125.4, 127.3, 127.7, 129.1, 129.9 (CH$_{Ar}$), 133.9, 134.7, 141.0, 141.8, 160.3 (C$_{Ar}$), 160.4 (C=O), 160.6 (C-7a), 163.3 (<u>C</u>O$_2$H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3275 (br w), 3036 (w), 1662 (s), 1563 (m), 1495 (m), 1348 (m), 1303 (m), 1272 (m), 1037 (s), 685 (m), 828 (m), 749 (s), 725 (s), 694 (s). MS (EI, 70 eV): *m/z* (%) = 477 (0.16) [M$^+$], 359 (100), 259 (85), 139 (79), 97 (28), 77 (20), 43 (94). Anal. Calcd for $C_{25}H_{23}N_3O_7$: C, 62.89; H, 4.86; N, 8.80. Found: C, 62.64; H, 5.09; N, 8.54.

2,6-Biphenyl-4-(perfluoroethyl)-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40j)

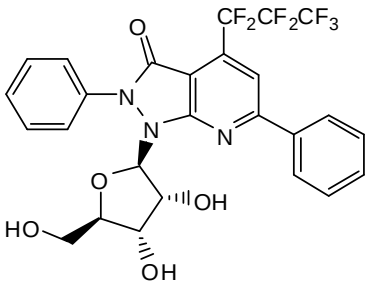


Starting from **37j** (332 mg, 0.5 mmol), **40j** was isolated via column chromatography as yellow solid (245 mg, 91%); mp 178-180 °C.

^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.92-2.99 (m, 1H, H$_a$-5'), 3.05-3.13 (m, 1H, H$_b$-5'), 3.58-3.63 (m, 1H, H-4'), 3.84-3.89

(m, 1H, H-3'), 4.50 (t, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 4.94-5.00 (m, 1H, H-2'), 5.07 (d, $^{3}J_{H,H}$ = 5.3 Hz, 1H, OH-3'), 5.40 (d, $^{3}J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.56 (d, $^{3}J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.39-7.44 (m, 1H, Ph), 7.53-7.64 (m, 7H, Ph), 8.18 (s, 1H, H-5), 8.30-8.33 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.2 (CH_2), 69.7, 70.8, 84.4, 94.0 (CH_{rib}), 106.8 (C-3a), 114.4 (C-5), 125.0, 127.3, 127.9, 129.0, 129.3, 131.5 (CH_{Ar}), 135.0, 136.4 (C_{Ar}), 135.7 (t, $^{2}J_{C,F}$ = 36.5 Hz, $\underline{C}CF_2CF_3$), 157.5 (C_{Ar}), 160.6 (C=O), 160.9 (C-7a). ^{19}F NMR (235 MHz, $CDCl_3$): δ = -82.49 (s, 3F, CF_3), -110.27 (s, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3195 (br), 2918 (w), 1695 (m), 1667 (m), 1590 (m), 1427 (w), 1386 (w), 1362 (m), 1324 (m), 1262 (w), 1202 (s), 1148 (m), 1093 (m), 1065 (m), 1053 (m), 1027 (m), 998 (s), 894 (w), 866 (m), 731 (s), 691 (m), 667 (m). MS (EI, 70 eV): *m/z* (%) = 537 (0.1) [M^+], 406 (70), 405 (100), 376 (39), 149 (26), 77 (42), 43 (17). HRMS (ESI): calcd $C_{25}H_{21}F_5N_3O_5$ ([M+1]$^+$) 538.1396, found 538.1397. Anal. Calcd for $C_{25}H_{20}F_5N_3O_5$: C, 55.87; H, 3.75; N, 7.82. Found: C, 56.04; H, 3.72; N, 7.78.

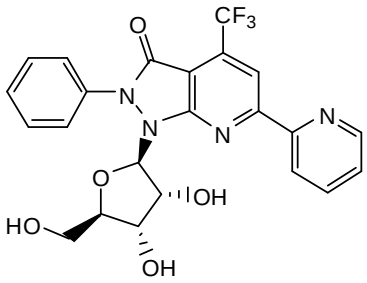
2,6-Biphenyl-4-(perfluoropropyl)-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40k)



Starting from **37k** (357 mg, 0.5 mmol), **40k** was isolated via column chromatography as yellow solid (249 mg, 85%); mp 146-148 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.93-3.01 (m, 1H, H_a-5'), 3.07-3.15 (m, 1H, H_b-5'), 3.58-3.64 (m, 1H, H-4'), 3.86-3.91 (m, 1H, H-3'), 4.50 (t, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 4.98-5.04 (m, 1H, H-2'), 5.08 (d, $^{3}J_{H,H}$ = 5.3 Hz, 1H, OH-3'), 5.42 (d, $^{3}J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.54 (d, $^{3}J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.39-7.45 (m, 1H, Ph), 7.54-7.63 (m, 7H, Ph), 8.23 (s, 1H, H-5), 8.30-8.33 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.1 (CH_2), 69.7, 70.8, 84.4, 93.9 (CH_{rib}), 105.7 (C-3a), 112.7 (C-5), 124.9, 127.3, 127.8, 129.0, 129.2, 131.4 (CH_{Ar}), 135.0 (t, $^{2}J_{C,F}$ = 36.1 Hz, $\underline{C}CF_2$), 135.3, 136.2, 157.8 (C_{Ar}), 160.7 (C=O), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.78 (t, $^{3}J_{F,F}$ = 10.2 Hz, 3F, CF_3), -108.64 (q, $^{3}J_{F,F}$ = 10.2 Hz, 2F, CF_2), -124.24 (t, $^{3}J_{F,F}$ = 21.5 Hz, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 587 (0.1) [M^+], 456 (20), 455 (100), 77 (19). HRMS (ESI): calcd $C_{26}H_{21}F_7N_3O_5$ ([M+1]$^+$) 588.13639, found 588.13645. Elemental analysis: Calculated for $C_{26}H_{20}F_7N_3O_5$: C, 56.11; H, 3.95; N, 6.33, found: C, 56.269; H, 3.966; N, 6.301.

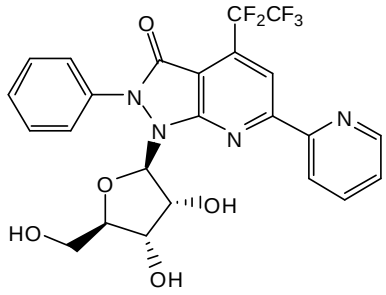
2-Phenyl-6-(pyridin-2-yl)-1-β-D-ribofuranozyl-4-(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (40l)



Starting from **37l** (307 mg, 0.5 mmol), **40l** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (227 mg, 93%); mp 267-268 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.00-3.07 (m, 1H, H_a-5'), 3.19-3.27 (m, 1H, H_b-5'), 3.60-3.65 (m, 1H, H-4'), 3.87-3.92 (m, 1H, H-3'), 4.55 (t, $^3J_{H,H}$ = 4.6 Hz, 1H, OH-5'), 4.90-4.93 (m, 1H, H-2'), 5.06 (d, $^3J_{H,H}$ = 4.9 Hz, 1H, OH-3'), 5.42-5.45 (m, 2H, OH-2', H-1'), 7.40-7.45 (m, 1H, Ar), 7.54-7.62 (m, 5H, Ar), 7.99 (td, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.9 Hz, 1H, Ar), 8.16 (s, 1H, H-5), 8.48 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.81-8.83 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.1 (CH_2), 69.7, 70.8, 84.4, 93.9 (CH_{rib}), 105.7 (C-3a), 112.7 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.7 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 124.9, 127.3, 127.8, 129.0, 129.2, 131.4 (CH_{Ar}), 135.0 (q, $^2J_{C,F}$ = 35.9 Hz, $\underline{C}CF_3$), 135.3, 136.2 (C_{Ar}), 150.1 (CH_{Ar}), 157.8 (C_{Ar}), 160.7 (C=O), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -66.55 (s). MS (EI, 70 eV): *m/z* (%) = 488 (0.1) [M^+], 357 (21), 356 (100), 355 (14), 251 (35), 203 (21), 78 (20), 77 (48), 51 (16). HRMS (ESI): calcd $C_{23}H_{20}F_3N_4O_5$ ([M+1]$^+$) 489.138, found 489.1383. Anal. Calcd for $C_{23}H_{19}F_3N_4O_5$: C, 56.56; H, 3.92; N, 11.47. Found: C, 56.78; H, 3.93; N, 11.41.

4-(Perfluoroethyl)-2-phenyl-6-(pyridin-2-yl)-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (40m)

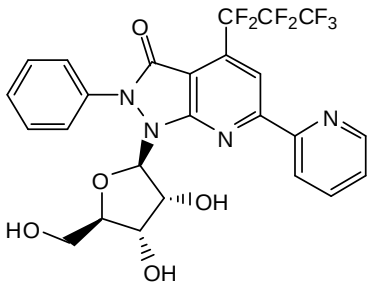


Starting from **37m** (333 mg, 0.5 mmol), **40m** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (245 mg, 93%); mp 205-207 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.04 (dd, $^2J_{H,H}$ = 11.5 Hz, $^3J_{H,H}$ = 6.0 Hz, 1H, H_a-5'), 3.25 (dd, $^2J_{H,H}$ = 11.5 Hz, $^3J_{H,H}$ = 5.4 Hz, 1H, H_b-5'), 3.58-3.64 (m, 1H, H-4'), 3.87 (t, $^3J_{H,H}$ = 4.7 Hz, 1H, OH-5'), 4.57 (br s, 1H, H-2'), 4.92 (br s, 1H, OH-3'), 5.04 (br s, 1H, OH-2'), 5.43 (d, $^3J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.41-7.46 (m, 1H, Ar), 7.54-7.63 (m, 5H, Ar), 7.99 (td, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.9 Hz, 1H, Ar), 8.18 (s, 1H, H-5), 8.50 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.81-8.84 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.3 (CH_2), 69.5, 70.7, 84.5, 94.2 (CH_{rib}), 111.5 (C-3a), 116.9 (t, $^3J_{C,F}$ = 3.7 Hz, C-5), 125.3, 125.4, 127.2, 127.6, 129.1, (CH_{Ar}), 134.9 (C_{Ar}), 136.5 (CH_{Ar}), 148.3 (t, $^2J_{C,F}$ = 25.4 Hz, $\underline{C}CF_2CF_3$), 149.9 (C_{Ar}), 150.1 (CH_{Ar}), 150.2 (C_{Ar}), 158.9 (C=O), 159.5 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -81.93 (s, 3F, CF_3), -113.88 - -117.02 (m, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3391 (br w), 2933 (w), 1666 (m), 1587

(m), 1469 (w), 1382 (w), 1354 (w), 1328 (m), 1261 (w), 1221 (m), 1189 (s), 1148 (m), 1114 (m), 1096 (m), 1045 (m), 1015 (s), 889 (m), 865 (m), 785 (m), 745 (s), 713 (m). MS (EI, 70 eV): *m/z* (%) = 538 (0.09) [M^+], 407 (33), 406 (100), 301 (45), 273 (16), 78 (11), 77 (34), 44 (30), 43 (19). HRMS (ESI): calcd $C_{24}H_{20}F_5N_4O_5$ ([M+1]$^+$) 539.1348, found 539.1352. Anal. Calcd for $C_{24}H_{19}F_5N_4O_5$: C, 53.54; H, 3.56; N, 10.41. Found: C, 53.68; H, 3.58; N, 10.38.

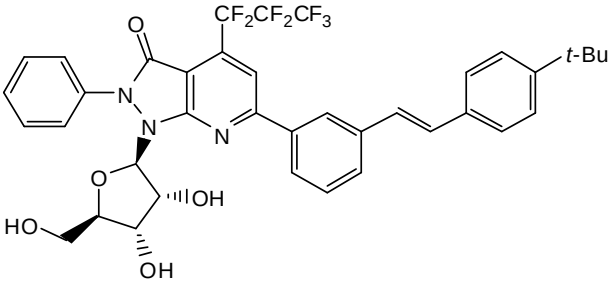
4-(Perfluoropropyl)-2-phenyl-6-(pyridin-2-yl)-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (40n)



Starting from **37n** (358 mg, 0.5 mmol), **40n** was isolated via column chromatography as yellow solid (271 mg, 92%); mp 178-180 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.03 (dd, $^2J_{H,H}$ = 11.0 Hz, $^3J_{H,H}$ = 5.9 Hz, 1H, H_a-5'), 3.24 (dd, $^2J_{H,H}$ = 11.0 Hz, $^3J_{H,H}$ = 4.5 Hz, 1H, H_a-5'), 3.57-3.62 (m, 1H, H-4'), 3.85 (br s, 1H, OH-5'), 4.56 (br s, 1H, H-2'), 4.86-4.90 (m, 1H, H-3'), 5.02-5.04 (m, 1H, OH-3'), 5.40 (br s, 1H, OH-2'), 5.43 (d, $^3J_{H,H}$ = 5.4 Hz, 1H, H-1'), 7.41-7.46 (m, 1H, Ar), 7.54-7.63 (m, 5H, Ar), 7.48-7.54 (m, 2H, Ar), 7.99 (td, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H, Ar), 8.16 (s, 1H, H-5), 8.51 (dt, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, Ar), 8.82-8.84 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.2 (CH_2), 69.5, 70.7, 84.5, 94.2 (CH_{rib}), 111.5 (C-3a), 117.2 (C-5), 125.3, 125.4, 127.2, 127.6, 126.1 (CH_{Ar}), 134.9 (C_{Ar}), 136.5 (CH_{Ar}), 149.8 (C_{Ar}), 150.1 (CH_{Ar}), 150.1 (C_{Ar}), 139.2 (t, $^2J_{C,F}$ = 24.0 Hz, $\underline{C}CF_2$), 158.9 (C=O), 159.4 (C-7a). ^{19}F NMR (235 MHz, DMSO-d_6): δ = -79.52 (t, $^3J_{F,F}$ = 9.2 Hz, 3F, CF_3), -113.27 (ddq, $^2J_{F,F}$ = 611.0 Hz, $^2J_{F,F}$ = 273.8 Hz, $^3J_{F,F}$ = 9.2 Hz, 2F, CF_2), -125.38 (s, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 588 (0.12) [M^+], 457 (57), 456 (100), 369 (39), 351 (35), 317 (76), 204 (21), 77 (46). HRMS (ESI): calcd $C_{25}H_{20}F_7N_4O_5$ ([M+1]$^+$) 589.13164, found 589.13184. Anal. Calcd for $C_{25}H_{19}F_7N_4O_5$: C, 51.03; H, 3.25; N, 9.52. Found: C, 51.19; H, 3.28; N, 9.56.

(*E*)-6-(3-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40o)

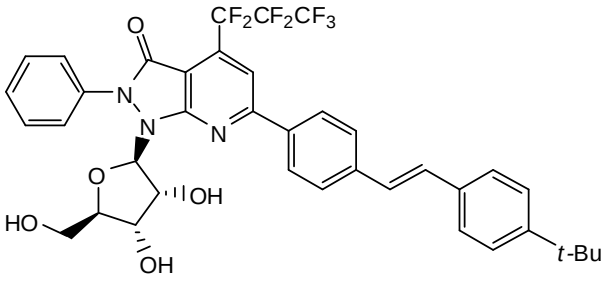


Starting from **37o** (436 mg, 0.5 mmol), **40o** was isolated via column chromatography as yellow solid (343 mg, 92%); mp 212-214 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.30

(s, 9H, CH_3), 3.01 (dt, $^2J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 5.3 Hz, 1H, H_a-5'), 3.11 (dt, $^2J_{H,H}$ = 11.1 Hz, $^3J_{H,H}$ = 5.3 Hz, 1H, H_b-5'), 3.64 (dd, $^3J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 5.3 Hz, 1H, H-4'), 3.93 (q, $^3J_{H,H}$ = 4.8 Hz, 1H, H-3'), 4.53 (t, $^3J_{H,H}$ = 5.0 Hz, 1H, OH-5'), 5.02-5.09 (m, 2H, H-2', OH-3'), 5.45 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.57 (d, $^3J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.34-7.47 (m, 5H, Ar, =CH), 7.54-7.65 (m, 7H, Ar, =CH), 7.87 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.21 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.26 (s, 1H, H-5), 8.49 (s, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 31.0 (CH_3), 34.4 ($\underline{C}(CH_3)_3$), 61.9 (CH_2), 69.8, 70.9, 84.5, 94.0 (CH_{rib}), 107.2 (C-3a), 114.7 (m, C-5), 125.0, 125.5, 125.9, 126.4, 126.8, 127.0, 127.3, 129.0, 129.1, 129.5, 129.7 (CH_{Ar}, =CH), 134.1 (C_{Ar}), 134.9 (t, $^2J_{C,F}$ = 26.1 Hz, $\underline{C}CF_3$), 135.4, 136.6, 138.3, 150.6, 157.4 (C_{Ar}), 160.5 (C=O), 160.8 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -79.38 (t, $^3J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.26 (q, $^3J_{F,F}$ = 9.2 Hz, 2F, CF_2), -123.82 (t, $^3J_{F,F}$ = 22.0 Hz, 2F, CF_2). MS (EI, 70 eV): *m/z* (%) = 745 (0.1) [M^+], 614 (41), 613 (100), 599 (24), 598 (81), 78 (25), 63 (31), 44 (24). HRMS (ESI): calcd $C_{38}H_{35}F_7N_3O_5$ ([M+1]$^+$) 746.24595, found 746.24587. Anal. Calcd for $C_{38}H_{34}F_7N_3O_5$: C, 61.21; H, 4.60; N, 5.64. Found: C, 61.41; H, 4.67; N, 5.66.

(*E*)-6-(4-(4-*tert*-butylstyryl)phenyl)-4-(perfluoropropyl)-2-phenyl-1-β-D-ribofuranozyl-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (40p)

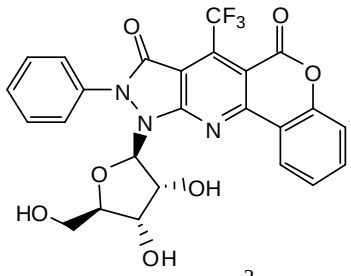


Starting from **37p** (436 mg, 0.5 mmol), **40p** was isolated via column chromatography as yellow solid (328 mg, 88%); mp 208-210 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.30 (s, 9H, CH_3), 2.97 (dd, $^2J_{H,H}$ = 11.2 Hz, $^3J_{H,H}$ = 5.6 Hz, 1H, H_a-5'), 3.12 (dd, $^2J_{H,H}$ = 11.2 Hz, $^3J_{H,H}$ = 5.6 Hz, 1H, H_b-5'), 3.63 (dd, $^3J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 5.6 Hz, 1H, H-4'), 3.85-3.89 (m, 1H, H-3'), 4.51 (br s, 1H, OH-5'), 4.94-5.08 (m, 2H, H-2', OH-3'), 5.37-5.44 (m, 1H, OH-2'), 5.56-5.59 (m, 1H, H-1'), 7.22-7.62 (m, 11H, =CH, =CH, Ar), 7.84 (d, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar), 8.20 (s, 1H, H-5), 8.36 (d, $^3J_{H,H}$ = 8.5 Hz, 2H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 31.0 (CH_3), 34.4 ($\underline{C}(CH_3)_3$), 61.2 (CH_2), 69.8, 70.9, 84.5, 94.0 (CH_{rib}), 106.9 (C-3a), 114.4 (t, $^3J_{C,F}$ = 8.9 Hz, C-5), 124.9, 125.2, 125.5, 126.6, 127.1, 127.2, 128.3, 128.4, 129.0, 130.5 (CH_{Ar}, =CH), 134.0, 134.7, 135.5, 140.4, 150.8, 157.5 (C_{Ar}), 160.4 (C=O), 160.6 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -79.40 (t, $^3J_{F,F}$ = 9.2 Hz, 3F, CF_3), -107.36 (q, $^3J_{F,F}$ = 9.2 Hz, 2F, CF_2), -123.89 (t, $^3J_{F,F}$ = 22.0 Hz, 2F, CF_2). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3390 (br w), 2960 (w), 1705 (m), 1699 (m), 1583 (s), 1495 (w), 1413 (w), 1363 (m), 1272 (w), 1229 (s), 1201 (m), 1180 (m), 1149 (m), 1113 (s), 1094 (m), 1028 (m), 966 (m), 951 (m), 878 (w), 834 (m), 734 (s), 694 (m), 662 (m), 559 (m). MS (EI, 70

eV): *m/z* (%) = 745 (0.1) [M^+], 613 (88), 259 (61), 157 (38), 139 (100), 97 (37), 77 (32), 43 (57). HRMS (ESI): calcd $C_{38}H_{35}F_7N_3O_5$ ([M+1]$^+$) 746.24595, found 746.24631. Anal. Calcd for $C_{38}H_{34}F_7N_3O_5$: C, 61.21; H, 4.60; N, 5.64. Found: C, 60.95; H, 4.62; N, 5.67.

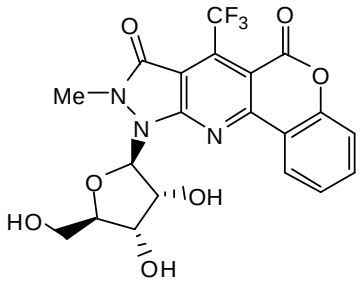
9-Phenyl-1-β-D-ribofuranozyl-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (40t)



Starting from **37t** (328 mg, 0.5 mmol), **40t** was isolated via column chromatography as yellow solid (251 mg, 95%); mp 215-216 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.74 (s, 3H, CH_3), 3.01-3.06 (m, 1H, H_a-5'), 3.15-3.20 (m, 1H, H_b-5'), 3.60-3.65 (m, 1H, H-4'), 3.86 (dd, $^2J_{H,H}$ = 8.9 Hz, $^3J_{H,H}$ = 5.1 Hz, 1H, H-3'), 4.56 (t, $^3J_{H,H}$ = 5.7 Hz, 1H, OH-5'), 4.83 (dd, $^2J_{H,H}$ = 11.6 Hz, $^3J_{H,H}$ = 5.9 Hz, 1H, H-2'), 5.04 (d, $^3J_{H,H}$ = 5.1 Hz, 1H, OH-3'), 5.35 (d, $^3J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.48 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, H-1'), 7.36-7.44 (m, 2H, Ph), 7.48-7.60 (m, 5H, Ph), 7.66-7.73 (m, 1H, Ph), 8.79-8.82 (m, 1H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 61.1 (CH_2), 69.5, 70.8, 85.0, 91.9 (CH_{rib}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 121.1 (q, $^1J_{C,F}$ = 275.9 Hz, CF_3), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.59 (s). Anal. Calcd for $C_{25}H_{18}F_3N_3O_7$: C, 56.72; H, 3.43; N, 7.94. Found: C, 56.84; H, 3.48; N, 7.78.

9-Methyl-1-β-D-ribofuranozyl-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (40u)

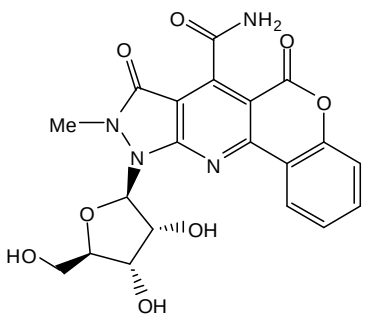


Starting from **37u** (297 mg, 0.5 mmol), **40u** was isolated via column chromatography as yellow solid (215 mg, 92%); mp 112-114 ^{o}C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.46-3.60 (m, 5H, NCH_3, H_a-5', H_b-5'), 3.88-3.89 (m, 1H, H-4'), 4.10 (br s, 1H, H-3'), 4.59 (t, $^3J_{H,H}$ = 4.7 Hz, 1H, OH-5'), 4.87 (br s, 1H, H-2'), 5.22-5.33 (m, 2H, OH-3', OH-2'), 6.15 (d, $^3J_{H,H}$ = 6.4 Hz, 1H, H-1'), 7.46-7.52 (m, 2H, Ar), 7.76 (t, $^3J_{H,H}$ = 7.6 Hz, 1H, Ar), 8.47 (t, $^3J_{H,H}$ = 7.6 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.9 (NCH_3), 61.1 (CH_2), 69.5, 70.8, 85.0, 91.9 (CH_{rib}), 109.6 (C-7a), 116.7 (CH_{Ar}), 117.8 (C-6a), 121.3 (q, $^1J_{C,F}$ = 278.9 Hz, CF_3), 125.0, 125.6, 134.2 (CH_{Ar}), 138.3 (q, $^2J_{C,F}$ = 37.5 Hz, $\underline{C}CF_3$), 152.5, 155.4, 156.6 (C_{Ar}), 157.9 (CO-6) 158.2 (CO-8), 159.8 (C-10a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -55.59 (s). HRMS (ESI): calcd $C_{20}H_{17}F_3N_3O_{10}$ ([M+1]$^+$) 468.10131,

found 468.10121. Anal. Calcd for $C_{20}H_{16}F_3N_3O_7$: C, 51.40; H, 3.45; N, 8.99. Found: C, 51.61; H, 3.50; N, 8.79.

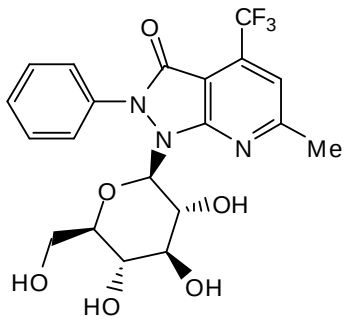
9-Methyl-1-β-D-ribofuranozyl-6,8-dioxo-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxamide (40w)



Starting from **37w** (292 mg, 0.5 mmol), **40w** was isolated via column chromatography as yellow solid (210 mg, 95%); mp 148-149 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.46-3.60 (m, 5H, NCH_3, H_a-5', H_b-5'), 3.88-3.89 (m, 1H, H-4'), 4.10 (br s, 1H, H-3'), 4.59 (t, $^3J_{H,H}$ = 4.7 Hz, 1H, OH-5'), 4.87 (br s, 1H, H-2'), 5.22-5.33 (m, 2H, OH-3', OH-2'), 6.15 (d, $^3J_{H,H}$ = 6.4 Hz, 1H, H-1'), 7.38-7.41 (m, 1H, Ar), 7.45-7.50 (m, 1H, Ar), 7.64-7.69 (m, 1H, Ar), 8.71-8.75 (m, 1H, Ar), 10.23 (br s, 2H, NH_2). ^{13}C NMR (62.9 MHz, DMSO-d_6): 31.0 (NCH_3), 62.4 (CH_2), 69.3, 71.8, 78.7, 90.4 (CH_{Rib}), 109.5 (C-7a), 117.6 (CH_{Ar}), 118.3 (C-6a), 125.6, 126.4, 134.3 (CH_{Ar}), 143.9, 153.2, 155.9, 158.9 (C_{Ar}), 159.1 (CO-6), 159.3 (CO-8), 164.3 (C-10a), 171.2 ($CONH_2$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3214 (br w), 2932 (w), 1704 (m), 1668 (m), 1610 (m), 1362 (m), 1332(w), 1262 (w), 1201 (s), 1157 (m), 1085 (m), 1053 (m), 979 (s), 894 (w), 871 (w), 731 (s), 658 (m). MS (EI, 70 eV): *m/z* (%) = 443 (0.2) [M+1$^+$], 442 (0.1) [M$^+$], 325 (12), 310 (66), 294 (21), 293 (100), 265 (41), 196 (30), 101 (45), 96 (20), 73 (20), 57 (34), 55 (21), 45 (54), 44 (31), 43 (61). HRMS (ESI): calcd $C_{20}H_{19}N_4O_8$ ([M+1]$^+$) 443.11978, found 443.12002. Anal. Calcd for $C_{20}H_{18}N_4O_8$: C, 54.30; H, 4.10; N, 12.66. Found: C, 54.19; H, 3.92; N, 12.21.

1-α-D-Glucopyranozyl-6-methyl-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41a)

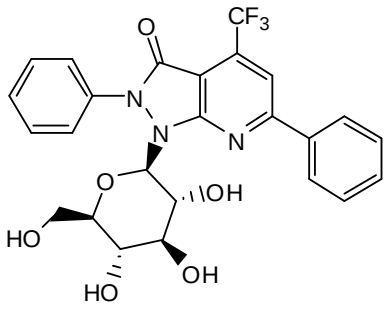


Starting from **38a** (312 mg, 0.5 mmol), **41a** was isolated via column chromatography as colorless solid (207 mg, 91%); mp 146-148 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.72 (s, 3H, CH_3), 2.74 (br s, 1H, H-5'), 3.06-3.22 (m, 3H, H-3', H_a-6', H_b-6') 3.56-3.62 (m, 1H, H-4'), 4.39 (t, $^3J_{H,H}$ = 5.8 Hz, 1H, OH-6'), 4.92 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, H-2'), 5.10 (d, $^3J_{H,H}$ = 4.7 Hz, 1H, H-1'), 5.33-5.35 (m, 1H, OH-4'), 5.65 (br s, 2H, OH-3', OH-2'), 7.35-7.40 (m, 1H, Ph), 7.47-7.52 (m, 2H, Ph), 7.58 (s, 1H, H-5), 7.61-7.64 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 25.0 (CH_3), 61.1 (CH_2), 69.7, 70.5, 77.3, 79.7, 89.1 (CH_{gl}), 102.6 (C-3a), 115.3 (q, $^3J_{C,F}$ = 5.0 Hz, CF_3C-5), 121.8 (q, $^1J_{C,F}$ = 274.6

Hz, CF_3), 125.8, 127.3, 128.5 (CH_{Ar}), 134.0 (q, $^2J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 135.5, 157.6 (C_{Ar}), 159.6 (C=O), 165.4 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.23 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3350 (br w), 2903 (w), 1674 (m), 1593 (m), 1493 (w), 1384 (m), 1337 (w), 1287 (w), 1254 (w), 1143 (s), 1119 (m), 1077 (s), 1025 (s), 896 (w), 755 (m), 702 (s), 575 (m). MS (EI, 70 eV): *m/z* (%) = 455 (0.3) [M^+], 294 (100), 293 (55), 273 (25), 264 (78), 85 (32), 77 (99), 73 (34), 57 (20), 43 (11). HRMS (ESI): calcd $C_{20}H_{21}F_3N_3O_6$ ([M+1]$^+$) 456.1377, found 456.1377. Anal. Calcd for $C_{20}H_{20}F_3N_3O_6$: C, 52.75; H, 4.43; N, 9.23. Found: C, 49.51; H, 4.28; N, 8.39.

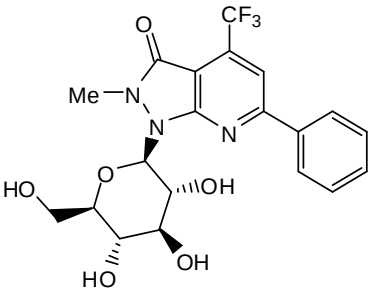
1-α-D-Glucopyranozyl-2,6-biphenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41b)



Starting from **38b** (343 mg, 0.5 mmol), **41b** was isolated via column chromatography as yellow solid (243 mg, 94%); mp 158-160 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.82-2.89 (m, 1H, H-5'), 3.09-3.22 (m, 3H, H_a-6', H_b-6', H-4'), 3.56-3.62 (m, 1H, H-3'), 4.39 (t, $^3J_{H,H}$ = 5.8 Hz, 1H, OH-6'), 4.94 (d, $^3J_{H,H}$ = 5.8 Hz, 1H, H-1'), 5.16-5.18 (m, 1H, H-2'), 5.50-5.51 (m, 1H, OH-4'), 5.66 (br s, 2H, OH-3', OH-2'), 7.40 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ph), 7.51-7.56 (m, 2H, Ph), 7.60-7.62 (m, 3H, Ph), 7.67-7.70 (m, 2H, Ph), 8.16 (s, 1H, H-5), 8.30-8.33 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.0 (CH_2), 69.8, 70.8, 77.3, 79.7, 89.2 (CH_{gl}), 104.2 (C-3a), 112.1 (q, $^3J_{C,F}$ = 5.1 Hz, C-5), 121.8 (q, $^1J_{C,F}$ = 274.2 Hz, CF_3), 125.6, 127.4, 128.0, 128.7, 129.2, 131.3 (CH_{Ar}), 135.2 (q, $^2J_{C,F}$ = 36.6 Hz, $\underline{C}CF_3$), 136.6, 155.0, 157.3 (C_{Ar}), 159.7 (CO), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d6): δ = -61.04 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3391 (br w), 2922 (w), 1681 (m), 1592 (m), 1494 (w), 1444 (w), 1372 (s), 1263 (m), 1145 (s), 1067 (s), 1042 (s), 883 (m), 775 (m), 751 (m), 690 (s). MS (EI, 70 eV): *m/z* (%) = 517 (0.10) [M^+], 355 (100), 326 (11), 77 (13), 71 (12), 57 (15), 43 (23). HRMS (ESI): calcd $C_{25}H_{23}F_3N_3O_6$ ([M+1]$^+$) 518.15335, found 518.15315. Anal. Calcd for $C_{25}H_{22}F_3N_3O_6$: C, 58.03; H, 4.29; N, 8.12. Found: C, 58.27; H, 4.51; N, 8.34.

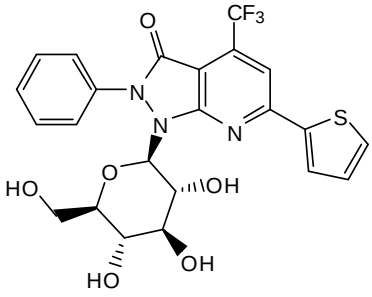
1-α-D-Glucopyranozyl-2-methyl-6-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41c)



Starting from **38c** (312 mg, 0.5 mmol), **41c** was isolated via column chromatography as yellow solid (212 mg, 93%); mp 199-202 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.20-3.28 (m, 1H, H-5'), 3.29-3.38 (m, 1H, H_a-6'), 3.43-3.47 (m, 1H, H_b-6'), 3.51-3.60 (m, 1H, H-4'), 3.53 (s, 3H, CH_3), 3.69 (br s, 1H, OH-4'), 3.76-3.82 (m, 1H, H-3'), 4.66 (t, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-6'), 5.10-5.13 (m, 2H, H-2', OH-3'), 5.18 (d, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-2'), 5.68 (d, $^{3}J_{H,H}$ = 8.9 Hz, 1H, H-1'), 7.58-7.61 (m, 3H, Ph), 8.02 (s, 1H, H-5), 8.28-8.31 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.7 (CH_3), 60.9 (CH_2), 69.6, 71.1, 77.2, 79.8, 88.0 (CH_{gl}), 103.3 (C-3a), 110.8 (C-5), 121.8 (q, $^{1}J_{C,F}$ = 274.2 Hz, CF_3), 127.8, 129.0, 131.0 (CH_{Ar}), 134.6 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 136.6, 158.5 (C_{Ar}), 158.5 (C=O), 160.3 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -60.97 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3271 (br w), 2907 (w), 1661 (m), 1638 (s), 1596 (m), 1417 (m), 1372 (m), 1253 (m), 1277 (m), 1258 (m), 1237 (m), 1145 (s), 1076 (s), 1050 (s), 1015 (s), 904 (m), 775 (s), 687 (s). MS (EI, 70 eV): *m/z* (%) = 455 (0.4) [M^+], 294 (98), 293 (48), 273 (31), 264 (77), 85 (25), 77 (100), 73 (21), 57 (20), 43 (48). HRMS (ESI): calcd $C_{20}H_{21}F_3N_3O_6$ ([M+1]$^+$) 456.1377, found 456.13728. Anal. Calcd for $C_{20}H_{20}F_3N_3O_6$: C, 52.75; H, 4.43; N, 9.23. Found: C, 52.54; H, 4.36; N, 8.99.

1-α-D-Glucopyranozyl-2-phenyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41e)

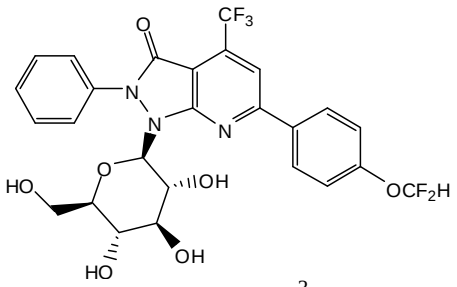


Starting from **38e** (346 mg, 0.5 mmol), **41e** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (236 mg, 90%); mp 140-142 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.19-3.25 (m, 1H, H-5'), 3.27-3.32 (m, 1H, H_a-6'), 3.40-3.46 (m, 1H, H_b-6'), 3.52-3.56 (m, 1H, H-4'), 3.64-3.67 (m, 1H, H-3'), 4.37-4.80 (m, 1H, H-2'), 4.65 (t, $^{3}J_{H,H}$ = 5.4 Hz, 1H, OH-6'), 5.10 (d, $^{3}J_{H,H}$ = 5.4 Hz, 2H, OH-4', OH-3'), 5.15 (d, $^{3}J_{H,H}$ = 5.4 Hz, 1H, OH-2'), 5.64 (d, $^{3}J_{H,H}$ = 9.0 Hz, 1H, H-1'), 7.30 (dd, $^{3}J_{H,H}$ = 4.9 Hz, $^{3}J_{H,H}$ = 4.0 Hz, 1H, Hetar), 7.38-7.44 (m, 1H, Ar), 7.53-7.60 (m, 4H, Ar), 7.96 (dd, $^{3}J_{H,H}$ = 4.9 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Hetar), 8.22 (s, 1H, H-5), 7.93 (dd, $^{3}J_{H,H}$ = 3.8 Hz, $^{4}J_{H,H}$ = 0.9 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 60.9 (CH_2), 69.6, 71.1, 77.2, 79.8, 88.0 (CH_{gl}),

104.8 (C-3a), 111.5 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.5 (q, $^{1}J_{C,F}$ = 274.5 Hz, CF_3), 124.7, 127.2, 129.1, 129.3, 130.4, 132.6 (CH_{Ar}), 135.0 (C_{Ar}), 135.2 (q, $^{2}J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 142.1, 156.4 (C_{Ar}), 157.6 (C=O), 160.3 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.21 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3365 (br w), 2918 (m), 2851 (w), 1682 (m), 1589 (m), 1537 (m), 1494 (w), 1489 (w), 1423 (m), 1378 (m), 1346 (m), 1265 (m), 1143 (s), 1039 (s), 854 (m), 753 (m), 713 (m). MS (EI, 70 eV): *m/z* (%) = 523 (0.1) [M^+], 362 (21), 361 (100), 332 (11), 77 (10). HRMS (ESI): calcd $C_{23}H_{21}F_3N_3O_6S$ ([M+1]$^+$) 524.10977, found 524.11001. Anal. Calcd for $C_{23}H_{20}F_3N_3O_6S$: C, 52.77; H, 3.85; N, 8.03. Found: C, 52.86; H, 3.87; N, 7.91.

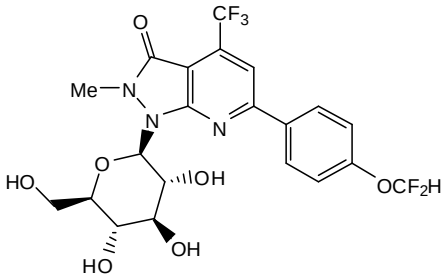
1-α-D-Glucopyranozyl-6-(4-(difluoromethoxy)phenyl)-2-phenyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41g)



Starting from **38g** (376 mg, 0.5 mmol), **41g** was isolated via column chromatography as yellow solid (280 mg, 96%); mp 148-150 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.82-2.89 (m, 1H, H-5'), 3.12-3.25 (m, 3H, H_a-6', H_b-6', H-4'), 3.56-3.62 (m, 1H, H-3'), 4.39 (t, $^{3}J_{H,H}$ = 5.6 Hz, 1H, OH-6'), 4.94 (d, $^{3}J_{H,H}$ = 5.6 Hz, 1H, H-1'), 5.16 (br s, 1H, H-2'), 5.50 (br s, 1H, OH-4'), 5.67 (br s, 2H, OH-3', OH-2'), 7.38-7.43 (m, 3H, Ar), 7.43 (t, $^{1}J_{H,H}$ = 73.7 Hz, 1H, OCF_2H), 7.51-7.56 (m, 2H, Ar), 7.66-7.69 (m, 2H, Ar), 8.17 (s, 1H, H-5), 8.39-8.42 (m, 2H, Ar). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 61.0 (CH_2), 69.7, 70.8, 77.3, 79.7, 89.2 (CH_{gl}), 104.0 (C-8), 112.0 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.0 Hz, OCF_2H), 118.7 (CH_{Ar}), 121.7 (q, $^{1}J_{C,F}$ = 274.6 Hz, CF_3), 125.6, 127.4, 128.7, 130.0, 133.3 (CH_{Ar}), 135.3 (q, $^{2}J_{C,F}$ = 35.2 Hz, $\underline{C}CF_3$), 153.3 (t, $^{3}J_{C,F}$ = 3.3 Hz, $\underline{C}OCF_2H$), 157.3 (C-6), 159.6 (CO), 160.1 (C-9). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.0 (s, 3F, CF_3), -82.8 (s, 2F, OCF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3389 (br w), 2927 (w), 1679 (w), 1594 (m), 1374 (m), 1264 (w), 1097 (m), 1048 (s), 841 (m). MS (EI, 70 eV): *m/z* (%) = 583 (0.05) [M^+], 421 (100), 392 (6), 77 (26). HRMS (ESI): calcd $C_{26}H_{23}F_5N_3O_7$ ([M+1]$^+$) 584.1451, found 584.1455. Anal. Calcd for $C_{26}H_{22}F_5N_3O_7$: C, 53.52; H, 3.80; N, 7.20. Found: C, 53.76; H, 3.69; N, 7.15.

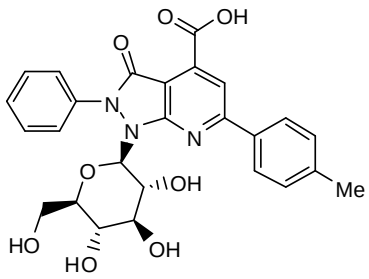
1-α-D-Glucopyranozyl-6-(4-(difluoromethoxy)phenyl)-2-methyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (41h)



Starting from **38h** (345 mg, 0.5 mmol), **41h** was isolated via column chromatography as yellow solid (245 mg, 94%); mp 229-231 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.19-3.25 (m, 1H, H-5'), 3.27-3.32 (m, 1H, H_a-6'), 3.40-3.46 (m, 1H, H_b-6'), 3.50 (s, 3H, NCH_3), 3.52-3.56 (m, 1H, H-4'), 3.64-3.67 (m, 1H, H-3'), 4.37-4.80 (m, 1H, H-2'), 4.65 (t, $^{3}J_{H,H}$ = 5.6 Hz, 1H, OH-6'), 5.10 (d, $^{3}J_{H,H}$ = 5.1 Hz, 2H, OH-4', OH-3'), 5.15 (d, $^{3}J_{H,H}$ = 5.3 Hz, 1H, OH-2'), 5.64 (d, $^{3}J_{H,H}$ = 8.7 Hz, 1H, H-1'), 7.33-7.36 (m, 2H, Ar), 7.40 (t, $^{2}J_{H,F}$ = 73.7 Hz, 1H, OCF_2H), 8.00 (s, 1H, H-5), 8.34-8.37 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 32.7 (NCH_3), 60.9 (CH_2), 69.6, 71.1, 77.2, 79.8, 88.0 (CH_{gl}), 103.3 (C-3a), 110.6 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.2 Hz, OCF_2H), 118.7 (CH_{Ar}), 126.2 (q, $^{1}J_{C,F}$ = 275.1 Hz, CF_3), 129.9 (CH_{Ar}), 133.4 (C_{Ar}), 134.7 (q, $^{2}J_{C,F}$ = 35.3 Hz, $\underline{C}CF_3$), 153.1 (t, $^{3}J_{C,F}$ = 3.2 Hz, $\underline{C}OCF_2H$), 158.5 (C_{Ar}), 158.6 (C=O), 159.3 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -60.95 (s, 3F, CF_3), -82.75 (s, 2F, OCF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3342 (br w), 2936 (w), 2889 (w), 1693 (m), 1659 (m), 1593 (m), 1374 (m), 1268 (m), 1226 (m), 1169 (m), 1143 (m), 1103 (s), 1068 (s), 1036 (s), 1012 (m), 841 (m), 671 (m). MS (EI, 70 eV): *m/z* (%) = 521 (0.4) [M^+], 360 (37), 359 (100), 331 (17), 85 (21), 73 (28), 61 (15), 57 (18), 43 (37). HRMS (ESI): calcd $C_{21}H_{21}F_5N_3O_7$ ([M+1]$^+$) 522.12942, found 522.13064. Anal. Calcd for $C_{21}H_{20}F_5N_3O_7$: C, 48.38; H, 3.87; N, 8.06. Found: C, 47.88; H, 3.90; N, 7.86.

1-α-D-Glucopyranozyl-3-oxo-2-phenyl-6-*p*-tolyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (41i)

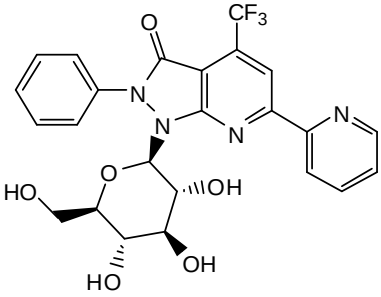


Starting from **38i** (345 mg, 0.5 mmol), **41i** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (241 mg, 97%); mp 188-190 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.43 (s, 3H, CH_3), 2.83 (br s, 1H, H-5'), 3.13-3.25 (m, 3H, H_a-6', H_b-6', H-4'), 3.34 (br s, 1H, H-3'), 3.58-3.63 (m, 1H, H-2'), 4.43 (t, $^{3}J_{H,H}$ = 5.7 Hz, 1H, OH-6'), 4.96 (d, $^{3}J_{H,H}$ = 5.5 Hz, 1H, OH-4'), 5.19 (d, $^{3}J_{H,H}$ = 4.3 Hz, 1H, OH-3'), 5.48 (br s, 1H, OH-2'), 5.64 (d, $^{3}J_{H,H}$ = 8.9 Hz, 1H, H-1'), 7.43 (m, 2H, Ar), 7.46-7.49 (m, 1H, Ar), 7.58 (t, $^{3}J_{H,H}$ = 7.6 Hz, 2H, Ar), 7.71 (d, $^{3}J_{H,H}$ = 7.6 Hz, 2H, Ar), 8.15-8.20 (m, 3H, Ar), 8.33 (s, 1H, H-5), 10.23 (s, 1H, CO_2H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 21.0 (CH_3), 61.1

(CH_2), 69.8, 70.7, 77.3, 79.6, 89.1 (CH_{gl}), 104.7 (C-3a), 115.7, 126.2, 127.4, 127.9, 128.7, 129.8 (CH_{Ar}), 134.3, 134.7, 141.0, 141.5, 159.4 (C_{Ar}), 160.1 (C=O), 160.5 (C-7a), 163.4 ($\underline{C}O_2H$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3306 (br w), 3065 (w), 2917 (w), 1667 (m), 1565 (s), 1493 (m), 1367 (m), 1278 (m), 1185 (w), 1069 (s), 1040 (s), 891 (w), 826 (m), 750 (m), 694 (m), 658 (m), 577 (s). MS (EI, 70 eV): *m/z* (%) = 508 (0.13) [M^++1], 507 (0.48) [M^+], 506 (0.47) [M^+-1], 345 (86), 344 (100), 299 (35), 77 (41). HRMS (ESI): calcd $C_{26}H_{27}N_4O_7$ ([M+1]$^+$) 507.1874, found 507.1877. Anal. Calcd for $C_{26}H_{25}N_3O_8$: C, 61.53; H, 4.97; N, 8.28. Found: C, 61.90; H, 5.02; N, 8.35.

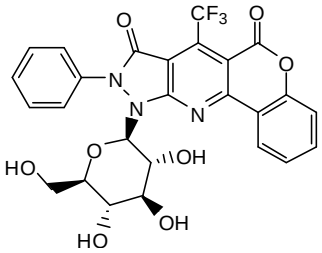
1-α-D-Glucopyranozyl-2-phenyl-6-(pyridin-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-b]pyridin-3(2*H*)-one (41l)



Starting from **38l** (344 mg, 0.5 mmol), **41l** was isolated via column chromatography as yellow solid (220 mg, 85%); mp 148-150 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.20-3.26 (m, 1H, H-5'), 3.27-3.32 (m, 1H, H_a-6'), 3.40-3.46 (m, 1H, H_b-6'), 3.52-3.56 (m, 1H, H-4'), 3.64-3.67 (m, 1H, H-3'), 4.37-4.80 (m, 1H, H-2'), 4.65 (t, $^3J_{H,H}$ = 5.6 Hz, 1H, OH-6'), 5.10 (d, $^3J_{H,H}$ = 5.1 Hz, 2H, OH-4', OH-3'), 5.15 (d, $^3J_{H,H}$ = 5.3 Hz, 1H, OH-2'), 5.64 (d, $^3J_{H,H}$ = 8.7 Hz, 1H, H-1'), 7.40-7.45 (m, 1H, Ar), 7.54-7.62 (m, 5H, Ar), 7.99 (td, $^3J_{H,H}$ = 7.8 Hz, $^4J_{H,H}$ = 1.9 Hz, 1H, Ar), 8.16 (s, 1H, H-5), 8.48 (d, $^3J_{H,H}$ = 7.8 Hz, 1H, Ar), 8.81-8.83 (m, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 60.9 (CH_2), 69.6, 71.1, 77.2, 79.8, 88.0 (CH_{rib}), 105.7 (C-3a), 112.9 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.7 (q, $^1J_{C,F}$ = 274.7 Hz, CF_3), 124.9, 127.3, 127.8, 129.0, 129.2, 131.4 (CH_{Ar}), 135.0 (q, $^2J_{C,F}$ = 35.9 Hz, $\underline{C}CF_3$), 135.3, 136.2 (C_{Ar}), 150.1 (CH_{Ar}), 157.8 (C_{Ar}), 160.7 (C=O), 161.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -66.55 (s). MS (EI, 70 eV): *m/z* (%) = 518 (0.1) [M^+], 357 (80), 356 (100), 355 (17), 252 (23), 251 (63), 223 (16), 203 (16), 77 (34). HRMS (ESI): calcd $C_{24}H_{22}F_3N_4O_6$ ([M+1]$^+$) 519.1486, found 519.1492. Anal. Calcd for $C_{24}H_{21}F_3N_4O_6$: C, 55.60; H, 4.08; N, 10.81. Found: C, 55.42; H, 4.10; N, 10.85.

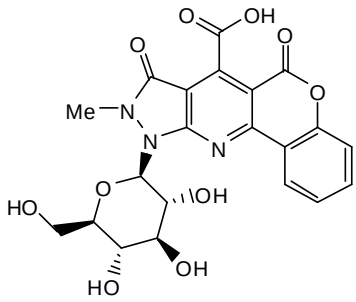
1-α-D-Glucopyranozyl-9-phenyl-7-(trifluoromethyl)-9,10-dihydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-6,8-dione (41t)



Starting from **38t** (292 mg, 0.5 mmol), **41t** was isolated via column chromatography as yellow solid (240 mg, 89%); mp 88-89 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.20-3.26 (m, 1H, H-5'), 3.28-3.31 (m, 1H, H_a-6'), 3.40-3.45 (m, 1H, H_b-6'), 3.52-3.56 (m, 1H, H-4'), 3.64-3.67 (m, 1H, H-3'), 4.37-4.80 (m, 1H, H-2'), 4.65 (t, $^3J_{H,H}$ = 5.7 Hz, 1H, OH-6'), 5.10 (d, $^3J_{H,H}$ = 5.1 Hz, 2H, OH-4', OH-3'), 5.15 (d, $^3J_{H,H}$ = 5.3 Hz, 1H, OH-2'), 5.64 (d, $^3J_{H,H}$ = 8.7 Hz, 1H, H-1'), 7.40-7.57 (m, 7H, Ar), 7.70-7.76 (m, 1H, Ar), 8.72 (d, $^3J_{H,H}$ = 7.6 Hz, 1H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.6 (CH_2), 67.7, 69.0, 73.4, 74.8, 85.8 (CH_{gl}), 95.7 (C-7a), 117.3 (CH_{Ar}), 117.7 (C-6a), 121.1 (q, $^1J_{C,F}$ = 276.0 Hz, CF_3), 125.2, 125.7, 126.7, 128.4, 129.6 (CH_{Ar}), 134.7 (C_{Ar}), 134.9 (CH_{Ar}), 153.3, 155.2, 156.5 (C_{Ar}), 156.9 (CO-6) 157.0 (CO-8), 161.2 (C-10a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -60.12 (s). MS (EI, 70 eV): *m/z* (%) = 559 (0.1) [M^+], 398 (32), 397 (100), 396 (41), 170 (58), 169 (99), 139 (20), 109 (88), 98 (21), 97 (42), 77 (49), 43 (58). HRMS (ESI): calcd $C_{26}H_{21}F_3N_3O_8$ ([M+1]$^+$) 560.12348, found 560.12352. Anal. Calcd for $C_{26}H_{20}F_3N_3O_8$: C, 55.82; H, 3.60; N, 7.51. Found: C, 55.61; H, 3.54; N, 7.55.

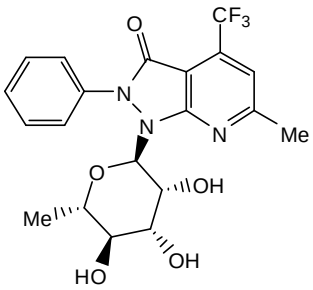
1-α-D-Glucopyranozyl-9-methyl-6,8-dioxo-6,8,9,10-tetrahydrochromeno[3,4-*e*]pyrazolo[3,4-*b*]pyridine-7-carboxylic acid (41w)



Starting from **38w** (328 mg, 0.5 mmol), **41w** was isolated via crystallization (CH_2Cl_2/MeOH) as yellow solid (199 mg, 91%); mp 124-125 °C.

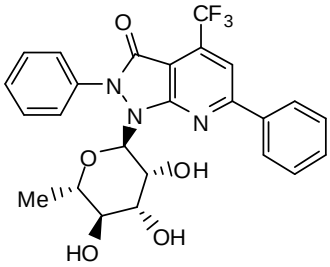
^{1}H NMR (250 MHz, DMSO-d_6): δ = 3.20-3.29 (m, 1H, H-5'), 3.38-3.44 (m, 2H, H_a-6', H_b-6'), 3.50 (s, 3H, NCH_3), 3.52-3.59 (m, 2H, H-4', H-3'), 3.75-3.81 (m, 1H, H-2'), 4.66 (t, $^3J_{H,H}$ = 4.8 Hz, 1H, OH-6'), 5.14-5.16 (m, 2H, OH-4', OH-3'), 5.29 (d, $^3J_{H,H}$ = 4.6 Hz, 1H, OH-2'), 5.75-5.80 (m, 1H, H-1'), 7.33-7.36 (m, 2H, Ar), 8.00 (s, 1H, H-5), 8.34-8.37 (m, 2H, Ar). ^{13}C NMR (62.9 MHz, DMSO-d_6): 22.5 (NCH_3), 62.9 (CH_2), 69.6, 71.0, 77.2, 79.8, 97.1 (CH_{Glu}), 107.4 (C-7a), 116.9 (CH_{Ar}), 118.3 (C-6a), 124.9, 125.8, 133.8 (CH_{Ar}), 144.1, 148.4, 152.6, 154.6 (C_{Ar}), 157.8 (CO-6), 159.4 (CO-8), 164.6 (C-10a), 171.5 ($\underline{C}O_2H$). MS (EI, 70 eV): *m/z* (%) = 437 (0.1) [M^+], 310 (67), 293 (100), 265 (44), 196 (37), 73 (20), 63 (21), 60 (23), 44 (64), 43 (29). HRMS (ESI): calcd $C_{21}H_{21}N_4O_9$ ([M+1]$^+$) 473.1303, found 473.1302. Anal. Calcd for $C_{21}H_{19}N_3O_{10}$: C, 53.28; H, 4.05; N, 8.88. Found: C, 53.60; H, 4.21; N, 8.69.

2,6-Biphenyl-1-α-L-rhamnopyranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42a)



Starting from **39a** (283 mg, 0.5 mmol), **42a** was isolated via column chromatography as colorless foam (198, 90%); mp 86-87 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.93 (d, $^{3}J_{H,H}$ = 6.6 Hz, 3H, $CH_{3\ (Rhamn)}$), 2.71 (s, 3H, CH_3), 3.21-3.25 (m, 1H, H-5'), 3.32 (t, $^{3}J_{H,H}$ = 3.1 Hz, 1H, H-4'), 3.70 (dd, $^{3}J_{H,H}$ = 5.4 Hz, $^{3}J_{H,H}$ = 3.3 Hz, 1H, H-3'), 4.61-4.67 (m, 1H, H-2'), 4.95 (d, $^{3}J_{H,H}$ = 4.2 Hz, 2H, OH-4', OH-3'), 5.04 (d, $^{3}J_{H,H}$ = 6.2 Hz, 1H, OH-2'), 5.53 (d, $^{3}J_{H,H}$ = 9.1 Hz, 1H, H-1'), 7.34-7.40 (m, 1H, Ph), 7.49-7.54 (m, 2H, Ph), 7.58-7.61 (m, 3H, H-5, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 16.7 ($CH_{3(rhamn)}$), 25.0 (CH_3), 65.6, 72.4, 72.7, 75.2, 82.1 (CH_{rhamn}), 103.7 (C-3a), 110.7 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.8 (q, $^{1}J_{C,F}$ = 274.9 Hz, CF_3), 127.7, 129.1, 131.0 (CH_{Ar}), 134.6 (q, $^{2}J_{C,F}$ = 36.1 Hz, $\underline{C}CF_3$), 136.7 (C_{Ar}), 158.3 (C-6), 158.8 (C=O), 160.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.28 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3401 (br w), 2933 (w), 1681 (m), 1674 (m), 1592 (m), 1489 (w), 1428 (w), 1381 (m), 1359 (m), 1243 (m), 1142 (s), 1116 (m), 1037 (s), 999 (m), 890 (m), 719 (m), 693 (m). HRMS (ESI): calcd $C_{20}H_{21}F_3N_3O_5$ ($[M+1]^+$) 440.14278, found 440.14272. Anal. Calcd for $C_{20}H_{20}F_3N_3O_5$: C, 54.67; H, 4.59; N, 9.56. Found: C, 54.77; H, 4.60; N, 9.52.

2,6-Biphenyl-1-α-L-rhamnopyranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42b)

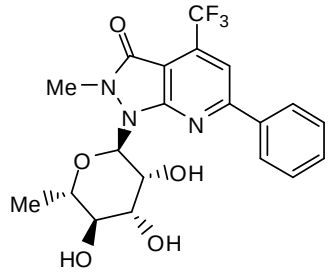


Starting from **39b** (314 mg, 0.5 mmol), **42b** was isolated via column chromatography as yellow solid (234, 93%); mp 142-144 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.97 (d, $^{3}J_{H,H}$ = 6.6 Hz, 3H, CH_3), 3.30-3.38 (m, 2H, H-4', OH-3'), 3.46-3.51 (m, 1H, H-5'), 3.82-3.83 (m, 1H, H-3'), 4.97-5.02 (m, 2H, H-2', OH-4'), 5.23 (d, $^{3}J_{H,H}$ = 6.3 Hz, 1H, OH-2'), 5.54 (d, $^{3}J_{H,H}$ = 9.1 Hz, 1H, H-1'), 7.41 (t, $^{3}J_{H,H}$ = 7.4 Hz, Ph), 7.54-7.67 (m, 7H, Ph), 8.18 (s, 1H, H-5), 8.34-8.36 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.5 (CH_3), 65.4, 73.4, 74.1, 74.2, 84.9 ($CH_{rhamnose}$), 104.9 (C-3a), 112.0 (C-5), 121.7 (q, $^{1}J_{C,F}$ = 275.0 Hz, CF_3), 125.1, 127.2, 127.9, 128.9, 129.1, 131.2 (CH_{Ar}), 135.2 (q, $^{2}J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 135.3, 136.5, 157.6 (C_{Ar}), 160.8 (C=O), 161.1 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.07 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3391 (br w), 2931 (w), 1674 (m), 1591 (s), 1494 (w), 1443 (w), 1373 (s), 1262 (m), 1142 (s), 1035 (s), 878 (m), 774 (m), 687 (s). MS

(EI, 70 eV): *m/z* (%) = 501 (1.4) [M^+], 355 (23), 273 (96), 171 (21), 153 (100), 111 (79), 83 (22), 77 (22), 43 (100). HRMS (ESI): calcd $C_{25}H_{23}F_3N_3O_5$ ([M+1]$^+$) 502.15843, found 502.15964. Anal. Calcd for $C_{25}H_{22}F_3N_3O_5$: C, 59.88; H, 4.42; N, 8.38. Found: C, 60.23; H, 4.24; N, 8.19.

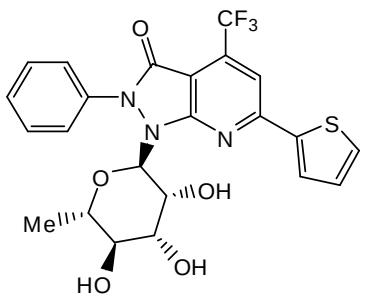
2-Methyl-6-phenyl-1-α-L-rhamnopyranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42c)



Starting from **39c** (283 mg, 0.5 mmol), **42c** was isolated via column chromatography as yellow solid (248 mg, 90%); mp 182-184 °C.

^{1}H NMR (300 MHz, DMSO-d_6): 1.40 (d, $^3J_{H,H}$ = 6.8Hz, 3H, CH_3 (rhamn)), 3.55 (s, 3H, NCH_3), 3.55-3.58 (m, 1H, H-4'), 3.76-3.78 (m, 1H, OH-3'), 3.92-3.93 (m, 1H, H-5'), 4.00-4.03 (m, 1H, H-3'), 4.33-4.43 (m, 1H, H-2'), 4.88 (d, $^3J_{H,H}$ = 6.6Hz, 1H, OH-2'), 5.11-5.14 (m, 2H, H-2', OH-4'), 6.07 (d, $^3J_{H,H}$ = 9.1Hz, 1H, H-1'), 7.56-7.58 (m, 2H, Ph), 8.00 (s, 1H, H-5), 8.23-8.26 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 16.7 (CH_3), 32.2 ($N\underline{C}H_3$), 65.6, 72.4, 72.7, 75.2, 82.1 (CH_{rhamn}), 103.7 (C-3a), 110.7 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.8 (q, $^1J_{C,F}$ = 275.1 Hz, CF_3), 127.7, 129.1, 131.0 (CH_{Ar}), 134.6 (q, $^2J_{C,F}$ = 35.2 Hz, $\underline{C}CF_3$), 136.7 (C_{Ar}), 158.3 (C-6), 158.8 (C=O), 160.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -60.95 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3367 (br w), 2938 (w), 1683 (m), 1595 (m), 1410 (w), 1369 (m), 1263 (m), 1230 (w), 1173 (m), 1113 (m), 1053 (s), 1034 (m), 1020 (m), 979 (m), 872 (m), 778 (m), 696 (s). MS (EI, 70 eV): *m/z* (%) = 439 (0.2) [M^+], 293 (100), 265 (37), 222 (16), 84 (89), 78 (84), 66 (98), 63 (88), 43 (29). HRMS (ESI): calcd $C_{20}H_{21}F_3N_3O_5$ ([M+1]$^+$) 440.14278, found 440.14274. Anal. Calcd for $C_{20}H_{20}F_3N_3O_5$: C, 54.67; H, 4.59; N, 9.56. Found: C, 54.52; H, 4.59; N, 9.64.

2-Phenyl-1-α-L-rhamnopyranozyl-6-(thiophen-2-yl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42e)

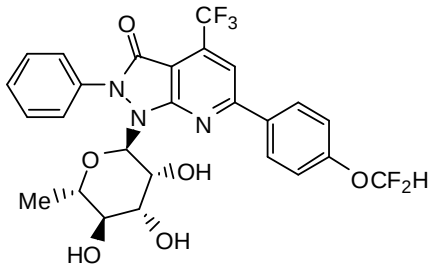


Starting from **39e** (317 mg, 0.5 mmol), **42e** was isolated via column chromatography as yellow solid (246 mg, 97%); mp 197-199 °C.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 0.96 (d, $^3J_{H,H}$ = 6.5 Hz, 3H, CH_3), 3.27 (br m, 1H, H-4'), 3.30-3.38 (m, 2H, H-4'), 3.43-3.52 (m, 1H, H-5'), 4.77 (br s, 1H, H-3'), 4.79-4.85 (m, 1H, H-2'), 4.97 (d, $^3J_{H,H}$ = 2.8 Hz, 2H, OH-3', OH-4'), 5.18 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.58 (d, $^3J_{H,H}$ = 9.0 Hz, 1H, H-1'), 7.27-7.31 (m, 1H, Ar/Hetar), 7.36-7.41 (m, 1H, Ar/Hetar), 7.50-764

(m, 4H, Ar/Hetar), 7.93 (d, $^{3}J_{H,H}$ = 4.9 Hz, 1H, Hetar), 8.15 (s, 1H, H-5), 8.30 (d, $^{3}J_{H,H}$ = 3.3 Hz, 1H, Hetar). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.7 (CH_3), 65.4, 73.7, 73.9, 74.7, 85.2 (CH_{rh}), 104.2 (C-3a), 110.8 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 122.6 (q, $^{1}J_{C,F}$ = 274.6 Hz, CF_3), 125.1, 127.1, 128.8, 129.2, 130.1, 132.6 (CH_{Ar}), 135.1 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 135.5, 142.4, 156.4 (C_{Ar}), 157.7 (C=O), 160.6 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -61.25 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3390 (br w), 3078 (w), 2915 (w), 1668 (w), 1591 (w), 1538 (w), 1496 (w), 1426 (w), 1379 (w), 1348 (w), 1268 (w), 1141 (m), 1115 (m), 1037 (m), 998 (w), 891 (w), 711 (s). MS (EI, 70 eV): *m/z* (%) = 633 (0.2) [M^+], 362 (22), 361 (100), 332 (17), 77 (19), 57 (17), 43 (19). HRMS (ESI): calcd $C_{23}H_{21}F_3N_3O_5S$ ([M+1]$^+$) 508.1149, found 508.1146. Anal. Calcd for $C_{23}H_{20}F_3N_3O_5S$: C, 54.43; H, 3.97; N, 8.28. Found: C, 54.61; H, 3.99; N, 8.25.

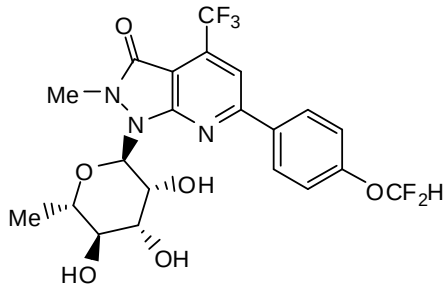
6-(4-(Difluoromethoxy)phenyl)-2-phenyl-1-α-L-rhamnopyranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42g)



Starting from **39g** (317 mg, 0.5 mmol), **42g** was isolated via column chromatography as yellow solid (250 mg, 88%); mp 120-122 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.96 (d, $^{3}J_{H,H}$ = 6.8 Hz, 3H, CH_3), 3.30-3.34 (m, 1H, H-4'), 3.42-3.48 (m, 1H, H-5'), 3.81-3.82 (m, 1H, H-3'), 4.94-5.02 (m, 3H, H-2', OH-3', OH-4'), 5.24 (d, $^{3}J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.52 (d, $^{3}J_{H,H}$ = 8.9 Hz, 1H, H-1'), 7.36-7.40 (m, 3H, Ar), 7.43 (t, $^{2}J_{F,H}$ = 73.7 Hz, 1H, OCF_2H), 7.52-7.58 (m, 2H, Ar), 7.64-7.68 (m, 2H, Ar), 8.18 (s, 1H, H-5), 8.41-8.44 (m, 2H, Ar). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 17.5 (CH_3), 65.5, 73.5, 74.2, 74.3, 85.0 (CH_{rhamn}), 104.8 (C-3a), 112.0 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.6 Hz, OCF_2H), 118.6 (CH_{Ar}), 121.8 (q, $^{1}J_{C,F}$ = 274.5 Hz, CF_3), 125.1, 127.2, 128.9, 130.0 (CH_{Ar}), 133.3, 135.3 (C_{Ar}), 135.3 (q, $^{2}J_{C,F}$ = 35.8 Hz, $\underline{C}CF_3$), 153.3 (t, $^{3}J_{C,F}$ = 3.3 Hz, $\underline{C}OCF_2H$), 157.6 (C-6), 160.0 (C=O), 160.8 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.11 (s, 3F, CF_3), -82.77 (s, 2F, OCF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3401 (br w), 3069 (w), 2934 (w), 1674 (m), 1593 (m), 1373 (m), 1263 (m), 1225 (m), 1112 (s), 1033 (s), 890 (m), 839 (m). MS (EI, 70 eV): *m/z* (%) = 567 (0.13) [M^+], 421 (100), 362 (22), 77 (27). HRMS (ESI): calcd $C_{26}H_{23}F_5N_3O_6$ ([M+1]$^+$) 568.1502, found 568.1506. Anal. Calcd for $C_{26}H_{22}F_5N_3O_6$: C, 55.03; H, 3.91; N, 7.40. Found: C, 53.18; H, 3.78; N, 7.32.

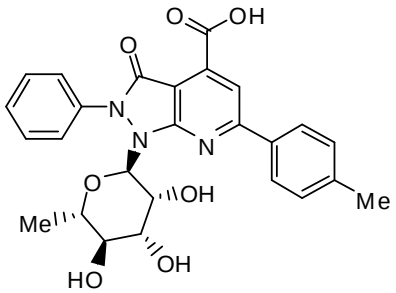
6-(4-(Difluoromethoxy)phenyl)-2-methyl-1-α-L-rhamnopyranozyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (42h)



Starting from **39h** (316 mg, 0.5 mmol), **42h** was isolated via column chromatography as yellow solid (230 mg, 91%); mp 235-237 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.40 (d, $^{3}J_{H,H}$ = 6.9 Hz, 3H, CH_3), 3.54 (s, 3H, NCH_3), 3.56-3.59 (m, 1H, H-5'), 3.92 (dd, $^{3}J_{H,H}$ = 6.9 Hz, $^{3}J_{H,H}$ = 3.4 Hz, 1H, H-4'), 3.97-4.04 (m, 1H, H-3'), 4.36-4.42 (m, 1H, H-2'), 4.88 (d, $^{3}J_{H,H}$ = 6.9 Hz, OH-3'), 5.13 (dd, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 3.9 Hz, 2H, OH-4', OH-2'), 6.05 (d, $^{3}J_{H,H}$ = 8.9 Hz, 1H, H-1'), 7.37 (d, $^{3}J_{H,H}$ = 8.9 Hz, 2H, Ar), 7.39 (t, $^{2}J_{F,H}$ = 73.7 Hz, 1H, OCF_2H), 8.02 (s, 1H, H-5), 8.33 (dt, $^{3}J_{H,H}$ = 8.9 Hz, $^{4}J_{H,H}$ = 1.9 Hz, 2H, Ar). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 16.7 (CH_3), 32.2 (NCH_3), 65.6, 72.3, 72.6, 75.2, 82.2 (CH_{rhamn}), 103.6 (C-3a), 110.6 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 116.1 (t, $^{1}J_{C,F}$ = 258.2 Hz, OCF_2H), 118.7 (CH_{Ar}), 121.9 (q, $^{1}J_{C,F}$ = 275.1 Hz, CF_3), 129.7 (CH_{Ar}), 133.4, (C_{Ar}), 134.7 (q, $^{2}J_{C,F}$ = 35.7 Hz, $\underline{C}CF_3$), 153.1 (t, $^{3}J_{C,F}$ = 3.4 Hz, $\underline{C}OCF_2H$), 158.2 (C-6), 158.7 (C=O), 159.2 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -61.24 (s, 3F, CF_3), -82.64 (s, 2F, OCF_2H). GC/MS (EI) m/z (%) = 506 (0.1) [M^+], 359 (100), 265 (30), 150 (36), 84 (68), 66 (72), 43 (22). HRMS (ESI): calcd $C_{21}H_{21}F_5N_3O_6$ ([M+1]$^+$) 506.1345, found 506.13435. Anal. Calcd for $C_{21}H_{20}F_5N_3O_6$: C, 49.91; H, 3.99; N, 8.31. Found: C, 49.79; H, 4.05; N, 8.34.

3-Oxo-2-phenyl-1-α-L-rhamnopyranozyl-6-*p*-tolyl-2,3-dihydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (42i)



Starting from **39i** (316 mg, 0.5 mmol), **42i** was isolated via crystallization (CH_2Cl_2/MeOH) as colorless solid (442 mg, 90%); mp 328-330 °C.

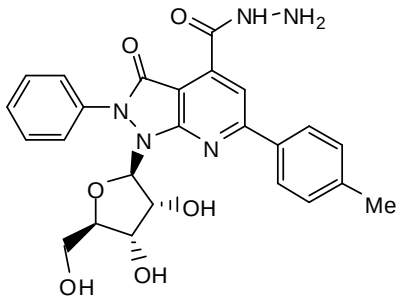
^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.95 (d, $^{3}J_{H,H}$ = 6.6 Hz, 3H, CH_3-6'), 2.40 (s, 3H, CH_3-4''), 3.29-3.32 (m, 1H, H-4'), 3.45-3.53 (m, 1H, H-5'), 3.81-3.82 (m, 1H, H-3'), 4.97-5.04 (m, 3H, H-2', OH-3', OH-4'), 5.23 (d, $^{3}J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.53 (d, $^{3}J_{H,H}$ = 8.9 Hz, 1H, H-1'), 7.38-7.41 (m, 2H, Ar), 7.44-7.47 (m, 1H, Ar), 7.55-7.60 (m, 2H, Ar), 7.66-7.68 (m, 2H, Ar), 8.15-8.18 (m, 3H, Ar), 8.33 (s, 1H, H-5), 10.22 (s, 1H, CO_2H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 17.6 (CH_3), 21.0 ($CH_{3rhamnose}$), 65.5, 73.6, 74.1, 74.4, 85.0 (CH_{rhamn}), 105.3 (C-3a), 115.7 (C-5), 125.7, 127.5, 127.7, 129.0, 129.8 (CH_{Ar}), 134.3, 134.8, 141.0, 141.6

(C_{Ar}), 163.4 (C=O), 160.4 (C-7a), 163.4 ($\underline{C}O_2H$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3333 (br w), 3183 (w), 3062 (w), 1668 (m), 1581 (m), 1496 (w), 1370 (m), 1277 (m), 1211 (m), 1062 (m), 1041 (m), 1024 (s), 979 (m), 745 (m), 690 (m), 657 (m), 605 (s), 571 (s). MS (EI, 70 eV): *m/z* (%) = 491 (0.4) [M^+], 344 (100), 315 (32), 301 (14), 272 (14), 168 (17), 77 (60). Anal. Calcd for $C_{26}H_{25}N_3O_7$: C, 63.54; H, 5.13; N, 8.55. Found: C, 63.64; H, 5.10; N, 8.26.

A.2.8. General procedure for synthesis of compounds 43-45

Compounds **37i, 38i, 39i** (0.5 mmol) were dissolved in 20mL MeOH and 5 mL of hydrazine hydrate was added. The mixture was stirred at room temperature overnight. The precipitate formed was filtrated, washed with CH_2Cl_2 and recrystallized from CH_2Cl_2/MeOH to afford bright-yellow solids.

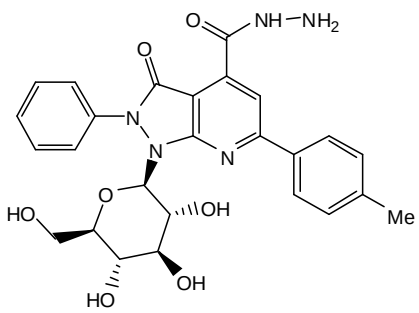
3-Oxo-2-phenyl-1-β-D-ribofuranozyl-6-p-tolyl-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine-4-carbohydrazide (43)



Starting from **37i** (309 mg, 0.5 mmol), **43** was isolated as yellow solid (245 mg, quant.); mp 238-239 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.42 (s, 3H, CH_3), 2.89-2.97 (m, 1H, H_a-5'), 3.07-3.14 (m, 1H, H_a-5'), 3.59 (q, $^3J_{H,H}$ = 4.9 Hz, 1H, H-4'), 3.87 (q, $^3J_{H,H}$ = 4.9 Hz, 1H, H-3'), 4.47 (t, $^3J_{H,H}$ = 4.9 Hz, 1H, OH-5'), 4.96 (d, $^3J_{H,H}$ = 4.0 Hz, 2H, NH_2), 5.02-5.08 (m, 2H, H-2', OH-3'), 5.42 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.50 (d, $^3J_{H,H}$ = 5.7 Hz, 1H, H-1'), 7.41-7.43 (m, 2H, Ar), 7.47-7.49 (m, 1H, Ar), 7.57-7.64 (m, 4H, Ar), 8.12-8.15 (m, 2H, Ar), 8.37 (s, 1H, H-5), 11.93 (t, $^3J_{H,H}$ = 4.0 Hz, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.9 (CH_3), 61.1 (CH_2), 69.7, 70.8, 84.3, 93.9 (CH_{rib}), 105.6 (C-3a), 115.6, 125.4, 127.3, 127.9, 129.1, 129.9 (CH_{Ar}), 133.9, 134.5, 140.0, 141.0, 160.0 (C_{Ar}), 160.3 (C=O), 160.6 (C-7a), 160.8 ($\underline{C}ONHNH_2$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3271 (br w), 2945 (w), 2837 (w), 1668 (m), 1643 (m), 1563 (s), 1488 (m), 1362 (m), 1273 (m), 1016 (s), 865 (m), 822 (m), 736 (s), 695 (s). MS (EI, 70 eV): *m/z* (%) = 491 (0.13) [M^+], 359 (100), 259 (88), 139 (69), 97 (28), 77 (18), 43 (91). HRMS (ESI): calcd $C_{25}H_{26}N_5O_6$ ([M+1]$^+$) 492.1878, found 492.1884. Anal. Calcd for $C_{25}H_{25}N_5O_6$: C, 61.09; H, 5.13; N, 14.25. Found: C, 61.34; H, 5.00; N, 14.07.

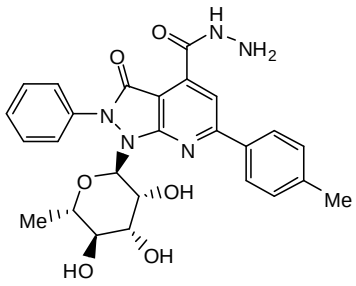
1-α-D-Glucopyranozyl-3-oxo-2-phenyl-6-p-tolyl-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine-4-carbohydrazide (44)



Starting from **38i** (345 mg, 0.5 mmol), **44** was isolated as yellow solid (260 mg, quant.); mp 270-271 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.42 (s, 3H, CH_3), 2.80 (br s, 1H, H-5'), 3.10-3.21 (m, 3H, H_a-6', H_b-6', H-4'), 3.41 (br s, 1H, H-3'), 3.56-3.62 (m, 1H, H-2'), 4.41 (t, $^3J_{H,H}$ = 5.6 Hz, 1H, OH-6'), 4.94 (d, $^3J_{H,H}$ = 5.5 Hz, 1H, OH-4'), 5.17 (d, $^3J_{H,H}$ = 3.4 Hz, 1H, OH-3'), 5.45 (br s, 1H, OH-2'), 5.62-5.65 (m, 3H, H-1', NH_2), 7.40-7.50 (m, 3H, Ar), 7.58 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, Ar), 7.70 (d, $^3J_{H,H}$ = 7.6 Hz, 2H, Ar), 8.15-8.20 (m, 2H, Ar), 8.42 (s, 1H, H-5), 13.25 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 21.0 (CH_3), 61.1 (CH_2), 69.8, 70.7, 77.3, 79.7, 89.1 (CH_{gl}), 104.2 (C-3a), 116.0 (C-5), 126.6, 127.5, 128.3, 128.9, 129.8 (CH_{Ar}), 134.3, 137.7, 140.1, 141.0, 158.6 (C_{Ar}), 158.6 (C=O), 159.1 (C-7a), 160.7 (CONHNH$_2$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3416 (br w), 2943 (w), 2798 (w), 1704 (w), 1651 (m), 1634 (m), 1568 (s), 1489 (w), 1364 (m), 1345 (m), 1280 (m), 1055 (s), 1012 (s), 821 (m), 740 (s), 701 (s). MS (EI, 70 eV): *m/z* (%) = 521 (2) [M$^+$], 399 (100), 384 (29), 359 (27), 355 (51), 344 (34), 326 (12), 301 (53), 239 (12), 141 (14), 77 (18), 69 (12), 60 (12), 44 (11). Anal. Calcd for $C_{26}H_{27}N_5O_7$: C, 59.88; H, 5.22; N, 13.43. Found: C, 60.09; H, 5.15; N, 12.77.

3-Oxo-2-phenyl-1-α-L-rhamnopyranozyl-6-p-tolyl-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine-4-carbohydrazide (45)



Starting from **39i** (316 mg, 0.5 mmol), **45** was isolated as yellow solid (252 mg, quant.); mp 252-253 °C.

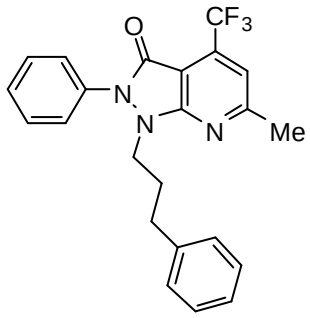
^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.94 (d, $^3J_{H,H}$ = 6.5 Hz, 3H, CH_3-6'), 2.41 (s, 3H, CH_3-4''), 3.29-3.33 (m, 1H, H-4'), 3.46-3.51 (m, 1H, H-5'), 3.80-3.81 (m, 1H, H-3'), 4.97-5.01 (m, 5H, H-2', OH-3', OH-4', NH_2), 5.24 (d, $^3J_{H,H}$ = 6.0 Hz, 1H, OH-2'), 5.52 (d, $^3J_{H,H}$ = 8.8 Hz, 1H, H-1'), 7.38-7.48 (m, 3H, Ar), 7.55-7.61 (m, 2H, Ar), 7.66-7.68 (m, 2H, Ar), 8.17 (d, $^3J_{H,H}$ = 8.2 Hz, 2H, Ar), 8.34 (s, 1H, H-5), 12.11 (br s, 1H, NH). ^{13}C NMR (62.8 MHz, DMSO-d_6): δ = 17.6, 21.0 (CH_3), 65.5, 73.5, 74.1, 74.4, 84.9 (CH_{Rhamn}), 104.7 (C-3a), 115.1 (C-5), 125.7, 127.5, 127.9, 129.0, 129.8 (CH_{Ar}), 134.3, 134.6, 139.9, 141.0, 160.2 (C_{Ar}), 160.4 (C=O), 160.5 (C-7a), 160.7 (CONHNH$_2$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3390 (br w), 2911 (w), 2810 (w), 1657 (m), 1651 (m), 1580 (s), 1494 (w), 1357 (m), 1285 (m), 1252 (w), 1184 (w), 1128 (w), 1047 (m), 979 (w), 822 (w), 728 (m), 693 (m). MS (EI, 70 eV):

m/z (%) = 505 (0.2) [M^+], 400 (80), 399 (100), 385 (52), 384 (82), 344 (52), 343 (76), 328 (20), 302 (64), 301 (88), 272 (32), 239 (71), 105 (19), 77 (62). HRMS (ESI): calcd $C_{26}H_{27}N_5O_6$ ([M+1]$^+$) 506.20214, found 506.20217. Anal. Calcd for $C_{26}H_{25}N_5O_6$: C, 61.77; H, 5.38; N, 13.85. Found: C, 61.92; H, 5.41; N, 13.81.

A.2.9. General procedure for synthesis of compounds 51

Under argon atmosphere, pyrazolo[3,4-b]pyridin-3-one **2** (1 mmol) and K_2CO_3 (414 mg, 3 mmol) were placed in a Schlenk flask and 15 mL of dry DMF was added. Appropriate alkyl bromide (1.1 mmol) was added dropwise the mixture was stirred at 90 ^oC for 4-10h (controlled by TLC). Then the solution was evaporated under reduced pressure, treated with H_2O, filtered, dried under reduced pressure and subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate).

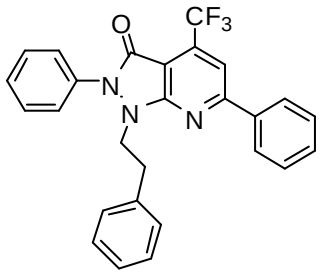
6-Methyl-2-phenyl-1-(3-phenylpropyl)-4-(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (51a)



Starting from **2a** (293 mg, 1 mmol) and (3-bromopropyl)benzene (219 mg, 1.1 mmol), **51a** was isolated as yellow oil (370 mg, 90%).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.63 (quin, $^3J_{H,H}$ = 7.6 Hz, 2H, $CH_2C\underline{H_2}CH_2$), 2.41 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, CH_2), 2.71 (s, 3H, CH_3), 4.04 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, NCH_2), 6.93-6.97 (m, 2H, Ph), 7.13-7.22 (m, 4H, Ph), 7.31-7.37 (m, 1H, Ph), 7.45-7.55 (m, 4H, H-5, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 25.5 (CH_3), 26.8, 32.7 (CH_2), 47.6 (NCH_2), 103.8 (C-3a), 114.7 (q, $^3J_{C,F}$ = 5.0 Hz, C-5), 121.8 (q, $^1J_{C,F}$ = 274.6 Hz, CF_3), 124.5, 126.2, 127.3, 128.1, 128.5, 129.4 (CH_{Ar}), 134.5 (C_{Ar}), 136.4 (q, $^2J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 140.5, 158.3 (C_{Ar}), 160.6 (C=O), 165.4 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.72 (s). Anal. Calcd for $C_{23}H_{20}F_3N_3O$: C, 67.14; H, 4.90; N, 10.21. Found: C, 67.41; H, 4.99; N, 10.16.

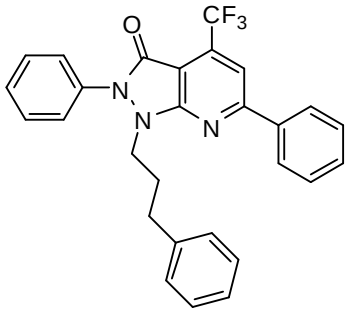
2,6-Biphenyl-1-phenethyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (51b)



Starting from **2c** (355 mg, 1 mmol) and (2-bromoethyl)benzene (204 mg, 1.1 mmol), **51b** was isolated as green solid (409 mg, 89%); mp 124-126 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.70 (t, $^{3}J_{H,H}$ = 7.2 Hz, 2H, CH_2), 4.38 (t, $^{3}J_{H,H}$ = 7.2 Hz, 2H, NCH_2), 6.94-6.97 (m, 2H, Ph), 7.00-7.11 (m, 3H, Ph), 7.34-7.40 (m, 1H, Ph), 7.50-7.60 (m, 7H, Ph), 7.71 (s, 1H, H-5), 8.08-8.12 (m, 2H, Ph). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 32.7 (CH_2), 49.3 (NCH_2), 104.7 (C-3a), 111.4 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.8 (q, $^{1}J_{C,F}$ = 275.0 Hz, CF_3), 124.4, 126.8, 127.3, 127.8, 128.5, 128.9, 129.2, 129.4, 131.1 (CH_{Ar}), 134.5 (C_{Ar}), 136.9 (q, $^{2}J_{C,F}$ = 36.0 Hz, $\underline{C}CF_3$), 137.4, 158.1 (C_{Ar}), 161.0 (C=O), 162.2 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.77 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3065 (w), 3003 (w), 1673 (s), 1591 (m), 1579 (m), 1494 (w), 1452 (m), 1423 (w), 1367 (m), 1358 (m), 1283 (m), 1269 (m), 1214 (w), 1181 (m), 1141 (s), 1133 (s), 1080 (w), 1057 (m), 878 (m), 775 (m), 758 (m), 715 (m), 694 (s). MS (EI, 70 eV): *m/z* (%) = 460 (11) [M^++1], 459 (43) [M^+], 369 (35), 368 (100), 355 (8), 105 (21), 104 (13), 77 (17), 43 (6). HRMS (ESI): calcd $C_{27}H_{20}F_3N_3O$ ([M+1]$^+$) 459.15530, found 459.15556. Anal. Calcd for $C_{27}H_{20}F_3N_3O$: C, 70.58; H, 4.39; N, 9.15. Found: C, 70.56; H, 4.28; N, 8.88.

2,6-Biphenyl-1-(3-phenylpropyl)-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (51c)

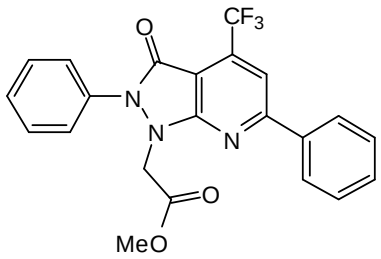


Starting from **2c** (355 mg, 1 mmol) and (3-bromopropyl)benzene (219 mg, 1.1 mmol), **51c** was isolated as green solid (417 mg, 88%); mp 112-114 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 (quin, $^{3}J_{H,H}$ = 7.5 Hz, 2H, $CH_2C\underline{H_2}CH_2$), 2.46 (t, $^{3}J_{H,H}$ = 7.5 Hz, 2H, CH_2), 4.13 (t, $^{3}J_{H,H}$ = 7.5 Hz, 2H, NCH_2), 6.96-7.00 (m, 2H, Ph), 7.14-7.22 (m, 3H, Ph), 7.33-7.39 (m, 1H, Ph), 7.49-7.59 (m, 7H, Ph), 7.81 (s, 1H, H-5), 8.05-8.11 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 26.8, 32.7 (CH_2), 47.6 (NCH_2), 104.6 (C-3a), 111.6 (q, $^{3}J_{C,F}$ = 5.0 Hz, C-5), 121.9 (q, $^{1}J_{C,F}$ = 275.0 Hz, CF_3), 124.5, 126.2, 127.3, 127.8, 128.2, 128.6, 129.2, 129.4, 131.2 (CH_{Ar}), 134.5 (C_{Ar}), 137.2 (q, $^{2}J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 137.3, 140.4, 158.2 (C_{Ar}), 160.7 (C=O), 162.4 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.66 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3061 (w), 2926 (w), 1690 (s), 1591 (m), 1581 (m), 1496 (w), 1444 (w), 1417 (w), 1373 (m), 1343 (m), 1274 (m), 1262 (m), 1141 (s), 1075 (w), 1048 (m), 1036 (m), 866 (w), 770 (m), 758 (s), 714 (m), 684 (s), 659 (m). MS (EI, 70 eV): *m/z* (%) = 474 (24) [M^++1], 743

(74) [M^+], 369 (23), 368 (100), 355 (35), 326 (12), 91 (60), 77 (38). HRMS (ESI): calcd $C_{28}H_{23}F_3N_3O$ ([M+1]$^+$) 474.17877, found 474.17869. Anal. Calcd for $C_{28}H_{22}F_3N_3O$: C, 71.03; H, 4.68; N, 8.87. Found: C, 71.31; H, 4.79; N, 8.89.

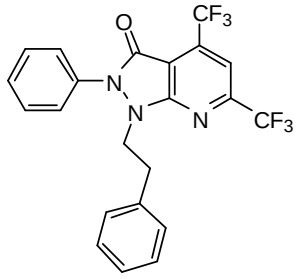
Methyl 2-(3-oxo-2,6-diphenyl-4-(trifluoromethyl)-2,3-dihydro-1H-pyrazolo[3,4-b]pyridin-1-yl)acetate (51d)



Starting from **2c** (355 mg, 1 mmol) and methyl 2-bromoacetate (168 mg, 1.1 mmol), **51d** was isolated as colorless solid (338 mg, 79%); mp 118-120 ^oC.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3H, CH_3), 4.31 (d, $^2J_{H,H}$ = 17.8 Hz, 1H, $CH_{2\text{-}a}$), 5.15 (d, $^2J_{H,H}$ = 17.8 Hz, 1H, $CH_{2\text{-}b}$), 7.31-7.37 (m, 1H, Ph), 7.42-7.52 (m, 7H, Ph), 7.64 (s, 1H, H-5), 8.02-8.06 (m, 2H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 48.6 (CH_2), 52.6 (OCH_3), 107.3 (C-3a), 110.5 (q, $^3J_{C,F}$ = 6.0 Hz, C-5), 122.6 (q, $^1J_{C,F}$ = 274.4 Hz, CF_3), 127.1, 127.4, 128.0, 129.0, 129.6, 130.9 (CH_{Ar}), 137.1, 140.1 (C_{Ar}), 140.8 (q, $^2J_{C,F}$ = 33.9 Hz, $\underline{C}CF_3$), 155.6 (C_{Ar}), 159.0 (NC=O), 160.1 (C-7a), 168.5 (OC=O). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -60.60 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3361 (w), 1699 (w), 1674 (m), 1650 (m), 1584 (m), 1566 (m), 1493 (m), 1466 (w), 1410 (m), 1368 (m), 1315 (w), 1260 (s), 1192 (w), 1143 9s), 1113 (m), 1074 (m), 961 (w), 918 (w), 864 (w), 778 (m), 714 (m), 688 (m). MS (EI, 70 eV): *m/z* (%) = 428 (21) [M^++1], 427 (100) [M^+], 407 (14), 381 (26), 368 (34), 277 (18), 223 (21), 104 (13), 77 (29), 44 (14). Anal. Calcd for $C_{22}H_{16}F_3N_3O_3$: C, 61.83; H, 3.77; N, 9.83. Found: C, 62.22; H, 3.90; N, 9.78.

1-Phenethyl-2-phenyl-4,6-bis(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (51e)

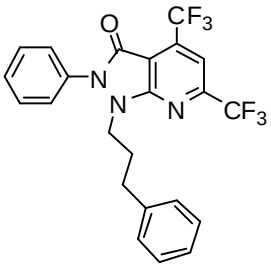


Starting from **2e** (347 mg, 1 mmol) and (2-bromoethyl)benzene (204 mg, 1.1 mmol), **51e** was isolated as green solid (392 mg, 87%); mp 123-125 ^oC.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.67 (t, $^3J_{H,H}$ = 6.8 Hz, 2H, CH_2), 4.42(t, $^3J_{H,H}$ = 6.8 Hz, 2H, NCH_2), 6.89-6.93 (m, 2H, Ph), 7.01-7.09 (m, 3H, Ph), 7.40-7.47 (m, 1H, Ph), 7.48 (s, 1H, H-5), 7.56-7.58 (m, 4H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.1, 32.6 (CH_2), 47.6 (NCH_2), 108.7 (C-3a), 110.4-110.6 (m, C-5), 120.6 (q, $^1J_{C,F}$ = 275.5 Hz, CF_3), 121.1 (q, $^1J_{C,F}$ = 275.5 Hz, CF_3), 125.1, 126.4, 128.0, 128.2, 128.6, 129.7 (CH_{Ar}), 133.6 (C_{Ar}), 136.4 (q, $^2J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 139.9 (C_{Ar}), 152.3 (q, $^2J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 156.6 (C=O), 158.8 (C-7a). ^{19}F NMR (282 MHz,

$CDCl_3$): δ = -62.70 (s), -68.10 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2947 (w), 1688 (m), 1593 (w), 1496 (w), 1463 (w), 1432 (w), 1352 (w), 1277 (s), 1211 (m), 1184 (m), 1139 (s), 1118 (s), 1090 (m), 1080 (m), 1056 (m), 1003 (w), 961 (w), 881 (m), 757 (m), 739 (m), 712 (m), 703 (s), 694 (m), 661 (m). MS (EI, 70 eV): *m/z* (%) = 452 (24) [M^++1], 451 (47) [M^+], 361 (17), 360 (100), 105 (48), 93 (15), 77 (28). HRMS (ESI): calcd $C_{22}H_{15}F_6N_3O$: ([M+1]$^+$) 451.11138, found 451.11162. Anal. Calcd for $C_{22}H_{15}F_6N_3O$: C, 58.54; H, 3.35; N, 9.31. Found: C, 58.74; H, 3.37; N, 9.28.

2-Phenyl-1-(3-phenylpropyl)-4,6-bis(trifluoromethyl)-1H-pyrazolo[3,4-b]pyridin-3(2H)-one (51f)

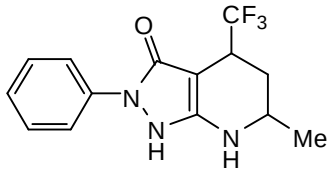


Starting from **2e** (347 mg, 1 mmol) and (3-bromopropyl)benzene (219 mg, 1.1 mmol), **51f** was isolated as yellow oil (424 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70 (quin, $^3J_{H,H}$ = 7.6 Hz, 2H, $CH_2C\underline{H_2}CH_2$), 2.44 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, CH_2), 4.12 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, NCH_2), 6.93-6.96 (m, 2H, Ph), 7.11-7.22 (m, 3H, Ph), 7.38-7.44 (m, 1H, Ph), 7.49-7.56 (m, 4H, Ph), 7.68 (s, 1H, H-5). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 27.1, 32.6 (CH_2), 47.6 (NCH_2), 108.7 (C-3a), 110.4-110.6 (m, C-5), 120.6 (q, $^1J_{C,F}$ = 275.5 Hz, CF_3), 121.1 (q, $^1J_{C,F}$ = 275.5 Hz, CF_3), 125.1, 126.4, 128.0, 128.2, 128.6, 129.7 (CH_{Ar}), 133.6 (C_{Ar}), 136.4 (q, $^2J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 139.9 (C_{Ar}), 152.3 (q, $^2J_{C,F}$ = 36.2 Hz, $\underline{C}CF_3$), 156.6 (C=O), 158.8 (C-7a). ^{19}F NMR (282 MHz, $CDCl_3$): δ = -62.49 (s), -67.93 (s). MS (EI, 70 eV): *m/z* (%) = 466 (18) [M^++1], 465 (52) [M^+], 390 (21), 389 (100), 105 (48), 93 (20), 77 (35), 43 (27). HRMS (ESI): calcd $C_{23}H_{18}F_6N_3O$: ([M+1]$^+$) 466.1298, found 466.1295. Anal. Calcd for $C_{23}H_{17}F_6N_3O$: C, 59.36; H, 3.68; N, 9.03. Found: C, 59.52; H, 3.71; N, 8.78.

A.2.10. General procedure for synthesis of compounds 59

Under argon atmosphere, pyrazolo[3,4-b]pyridin-3-one **2** (1 mmol) and Hatszch ester (1.0 g, 4 mmol), and PTSA (19.0 mg, 10 mol%) were placed in a flask, dissolved in benzene (50 mL) and heated at 60 ^{o}C for 16-72 h (controlled by TLC). Afterwards, the solution was evaporated under reduced pressure and subjected to column chromatography (silica gel; eluent: n-heptane/ethylacetate). After isolation from column, products **59** were recrystallized from i-PrOH.

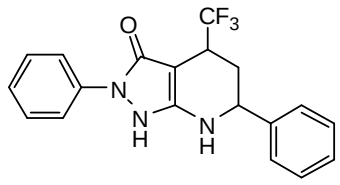
6-Methyl-2-phenyl-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (59a)



Starting from **2a** (293 mg, 1 mmol), **59a** was isolated as pale brown solid (285 mg, 96%); mp 156-158 °C.

^{1}H NMR (300 MHz, DMSO-d_6,): δ = 1.22 (d, $^{3}J_{H,H}$ = 6.4 Hz, 3H, CH_3), 1.45 (dt, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 10.8 Hz, 1H, H_a-5), 2.11 (ddd, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 6.0 Hz, $^{3}J_{H,H}$ = 2.3 Hz, 1H, H_b-5), 3.40-3.45 (m, 1H, H-6), 3.48-3.59 (m, 1H, H-4), 7.03 (t, $^{3}J_{H,H}$ = 7.5 Hz, 1H, Ph), 7.06 (s, 1H, H-7), 7.34 (t, $^{3}J_{H,H}$ = 7.5 Hz, 2H, Ph), 7.59 (d, $^{3}J_{H,H}$ = 7.5 Hz, 2H, Ph), 9.74 (s, 1H, H-1). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.7 (CH_3), 31.0 (CH_2), 34.9 (q, $^{2}J_{C,F}$ = 28.8 Hz, $\underline{C}CF_3$), 46.0 ($\underline{C}CH_3$), 76.8 (C-3a), 117.7, 122.5 (CH_{Ar}), 127.1 (q, $^{1}J_{C,F}$ = 280.0 Hz, CF_3), 128.5 (CH_{Ar}), 139.8 (C-1'), 158.9 (C=O), 163.7 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -67.26 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3122 (w), 2973 (w), 1568 (s), 1557 (s), 1495 (m), 1259 (m), 1143 (m), 1116 (s), 749 (m), 690 (s). MS (EI, 70 eV): *m/z* (%) = 298 (23) [M^++1], 297 (100) [M^+], 282 (39) [M^+-CH_3], 200 (17), 172 (18), 122 (23), 105 (22), 77 (50), 51 (7). HRMS (ESI): calcd $C_{14}H_{14}F_3N_3O$ ([M+1]$^+$) 297.10835, found 297.108682. Anal. Calcd for $C_{14}H_{14}F_3N_3O$: C, 56.56; H, 4.75; N, 14.14. Found: C, 56.82; H, 4.95; N, 13.85.

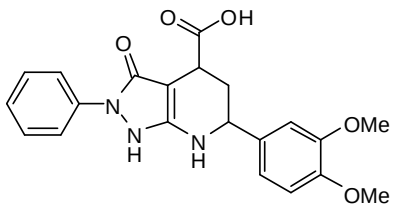
2,6-Diphenyl-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (59b)



Starting from **2c** (355 mg, 1 mmol), **59b** was isolated as pale brown solid (252 mg, 70%); mp 121-123 °C.

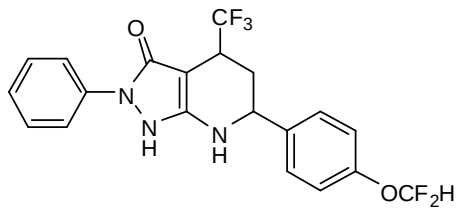
^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.85 (dt, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 9.8 Hz, 1H, H_a-5), 2.22 (ddd, $^{2}J_{H,H}$ = 13.0 Hz, $^{3}J_{H,H}$ = 5.8 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, H_b-5), 3.60-3.73 (m, 1H, H-6), 4.56 (dd, $^{3}J_{H,H}$ = 9.8 Hz, $^{3}J_{H,H}$ = 2.7 Hz, 1H, H-4), 7.05 (t, $^{3}J_{H,H}$ = 7,4 Hz, 1H, Ph), 7.32-7.45 (m, 7H, Ar), 7.49 (s, 1H, H-7), 7.61 (d, $^{3}J_{H,H}$ = 7,4 Hz, 2H, Ph), 9.88 (s, 1H, H-1). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 32.1 (CH_2), 35.0 (q, $^{2}J_{C,F}$ = 29.5 Hz, $\underline{C}CF_3$), 54.0 (C-6), 77.0 (C-3a), 117.8, 122.6, 126.6 (CH_{Ar}), 126.9 (q, $^{1}J_{C,F}$ = 280.0 Hz, CF_3), 127.7, 128.5 (CH_{Ar}), 139.6, 141.7 (C_{Ar}), 159.0 (C=O), 163.6 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -67.15 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3031 (w), 2860 (w), 1592 (m), 1568 (m), 1556 (m), 1495 (m), 1257 (m), 1150 (m), 1115 (s), 747 (s), 697 (s). MS (EI, 70 eV): *m/z* (%) = 360 (25) [M^++1], 359 (100) [M^+], 174 (16), 122 (16), 105 (25), 77 (41), 51 (6). HRMS (ESI): calcd $C_{19}H_{17}F_3N_3O$ ([M+1]$^+$) 360.13182, found 360.13184. Anal. Calcd for $C_{19}H_{16}F_3N_3O$: C, 63.51; H, 4.49; N, 11.69. Found: C, 63.76; H, 4.37; N, 11.33.

6-(3,4-Dimethoxyphenyl)-3-oxo-2-phenyl-2,3,4,5,6,7-hexahydro-1H-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (59c)



Starting from **2m** (405 mg, 1 mmol), **59c** was isolated as colorless solid (186 mg, 47%); mp 228-230 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.90 (dt, $^{2}J_{H,H}$ = 13.1 Hz, $^{3}J_{H,H}$ = 10.5 Hz, 1H, H-5$_a$), 2.23 (ddd, $^{2}J_{H,H}$ = 13.1 Hz, $^{3}J_{H,H}$ = 5.6 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, H-5$_b$), 3.61 (dd, $^{3}J_{H,H}$ = 10.5 Hz, $^{3}J_{H,H}$ = 5.6 Hz, 1H, H-6), 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.47 (dd, $^{3}J_{H,H}$ = 10.5 Hz, $^{3}J_{H,H}$ = 2.8 Hz, 1H, H-4), 6.92-6.96 (m, 2H, Ar), 7.01 (s, 1H, 2'-H), 7.09 (t, $^{3}J_{H,H}$ = 7,4 Hz, 1H, Ph), 7.38 (t, $^{3}J_{H,H}$ = 7,9 Hz, 2H, Ar), 7.42 (br s, 1H, H-7), 7.61 (d, $^{3}J_{H,H}$ = 7,9 Hz, 2H, Ar), 10.23 (br s, 1H, H-1). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ = 35.7 (CH_2), 36.4 (C-6), 55.0 (C-4), 55.5, 55.6 (OCH_3), 81.0 (C-3a), 110.4, 111.7, 118.0, 118.7, 123.1, 128.7 (CH_{Ar}), 134.3, 138.9, 148.3, 148.8 (C_{Ar}), 157.3 (C=O), 164.2 (C-7a), 173.7 (CO_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3226 (w), 3100 (w), 2953 (w), 1722 (m), 1602 (m), 1574 (s), 1514 (m), 1495 (m), 1267 (m), 1230 (m), 1172 (m), 1152 (m), 1092 (m), 1026 (m), 748 (m). MS (EI, 70 eV): *m/z* (%) = 396 (52) [M^++1], 395 (98) [M^+], 351 (74), 350 (77), 349 (100), 347 (68), 334 (59), 257 (21), 231 (81), 221 (25), 177 (71), 175 (76), 164 (69), 151 (26), 93 (22), 91 (22), 77 (50), 73 (27), 60 (27), 44 (21), 43 (16). HRMS (ESI): calcd $C_{21}H_{22}N_3O_5$ ([M+1]$^+$) 396.1554, found 396.1554. Anal. Calcd for $C_{21}H_{21}N_3O_5$: C, 63.79; H, 5.35; N, 10.63. Found: C, 63.99; H, 3.37; N, 10.77.

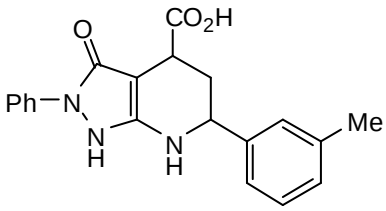
6-(4-(Difluoromethoxy)phenyl)-2-phenyl-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one (59d)



Starting from **2o** (421 mg, 1 mmol), **59d** was isolated as pale brown solid (276 mg, 65%); mp 114-116 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.91 (dt, $^{2}J_{H,H}$ = 13.2 Hz, $^{3}J_{H,H}$ = 10.0 Hz, 1H, H$_a$-5), 2.27 (ddd, $^{2}J_{H,H}$ = 13.2 Hz, $^{3}J_{H,H}$ = 5.9 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, H$_b$-5), 3.64-3.78 (m, 1H, H-6), 4.64 (dd, $^{3}J_{H,H}$ = 10.0 Hz, $^{3}J_{H,H}$ = 3.2 Hz, 1H, H-4), 7.11 (t, $^{3}J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.25-7.27 (m, 2H, Ar), 7.30 (t, $^{1}J_{F,H}$ = 74.1 Hz, 1H, OCF_2H), 7.38-7.43 (m, 2H, Ar), 7.52-7.55 (m, 3H, Ar, H-7), 7.64-7.68 (m, 2H, Ar), 9.96 (s, 1H, H-1). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 31.9 (CH_2), 35.0 (q, $^{2}J_{C,F}$ = 29.9 Hz, $\underline{C}CF_3$), 53.3 (C-6), 77.2 (C-3a), 116.4 (t, $^{1}J_{C,F}$ = 257.8 Hz, OCF_2H), 117.9, 118.9, 122.8, 128.4, 128.6 (CH_{Ar}), 127.0 (q, $^{1}J_{C,F}$ = 280.1 Hz, CF_3), 138.8, 139.6 (C_{Ar}), 148.8 (C=O), 150.3 (t, $^{3}J_{C,F}$ = 3.3 Hz, $\underline{C}OCF_2H$), 158.8 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -67.10 (s, 3F, CF_3), -82.03 (s, 2F, OCF_2H). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3067 (w), 2979 (w), 1574 (m), 1556 (m), 1497 (m), 1369 (w), 1335 (w), 1259 (m), 1219 (m), 1176 (m), 1112 (s), 1032

(s), 748 (m), 691 (m). MS (EI, 70 eV): *m/z* (%) = 426 (24) [M^++1], 425 (100) [M^+], 282 (5), 255 (8), 174 (27), 122 (10), 105 (10), 77 (30), 51 (5). HRMS (ESI): calcd $C_{20}H_{16}F_5N_3O_2$: ([M+1]$^+$) 425.11572, found 425.116207. Anal. Calcd for $C_{20}H_{16}F_5N_3O_2$: C, 56.47; H, 3.79; N, 9.88. Found: C, 56.59; H, 3.62; N, 9.65.

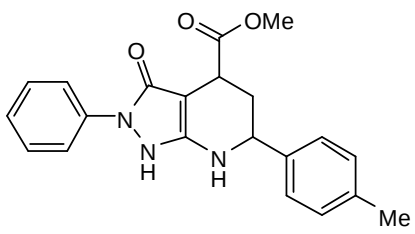
3-Oxo-2-phenyl-6-*m*-tolyl-2,3,4,5,6,7-hexahydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (59e)



Starting from **2s** (373 mg, 1 mmol), **59e** was isolated as pale brown solid (192 mg, 51%); mp 250-251 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.86 (dt, $^2J_{H,H}$ = 13.1 Hz, $^3J_{H,H}$ = 10.5 Hz, 1H, H_a-5), 2.17 (ddd, $^2J_{H,H}$ = 13.1 Hz, $^3J_{H,H}$ = 5.7 Hz, $^3J_{H,H}$ = 2.6 Hz, 1H, H_b -5), 2.33 (s, 3H, CH_3), 3.48 (dd, $^3J_{H,H}$ = 10.5 Hz, $^3J_{H,H}$ = 5.7 Hz, 1H, H-6), 4.51 (dd, $^3J_{H,H}$ = 10.5 Hz, $^3J_{H,H}$ = 2.6 Hz, 1H, H-4), 7.06-7.15 (m, 2H, H-7, Ar), 7.18-7.30 (m, 3H, Ar), 7.35-7.40 (m, 2H, Ar), 7.47-7.50 (m, 1H, Ar), 7.59-7.62 (m, 2H, Ar), 10.25 (s, 1H, H-1). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 21.1 (CH_3), 35.7 (CH_2), 36.4 (CH-6), 55.5 (CH-4), 80.9 (C-3a), 118.0, 123.2, 123.8, 127.2, 128.3, 128.4, 128.7 (CH_{Ar}), 137.6, 138.9, 141.9 (C_{Ar}), 157.3 (C=O), 164.2 (C-7a), 173.7 ($\underline{C}O_2H$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3044 (w), 2981 (w), 2855 (w), 1651 (w), 1634 (m), 1589 (w), 1548 (w), 1498 (m), 1379 (m), 1347 (m), 1230 (m), 1092 (w), 1012 (w), 887 (w), 790 (m), 752 (m), 706 (m), 690 (m). MS (EI, 70 eV): *m/z* (%) = 350 (7) [M^++1], 349 (35) [M^+], 304 (17), 303 (69), 301 (11), 78 (97), 63 (100), 61 (12), 45 (11). HRMS (ESI): calcd $C_{20}H_{19}N_3O_3$ ([M+1]$^+$) 349.14339, found 349.142380. Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.81; H, 5.57; N, 11.89.

Methyl 3-oxo-2-phenyl-6-*p*-tolyl-2,3,4,5,6,7-hexahydro-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylate (59f)

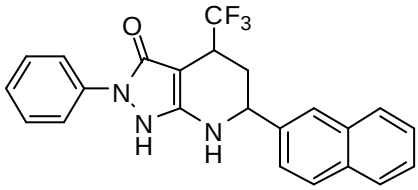


Starting from **2u** (359 mg, 1 mmol), **59f** was isolated as colorless solid (265 mg, 73%); mp 218-220 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.98 (dt, $^2J_{H,H}$ = 12.9 Hz, $^3J_{H,H}$ = 8.0 Hz, 1H, H_a-5), 2.17 (ddd, $^2J_{H,H}$ = 12.9 Hz, $^3J_{H,H}$ = 6.0 Hz, $^3J_{H,H}$ = 3.0 Hz, 1H, H-5$_b$), 2.29 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 3.48 (dd, $^3J_{H,H}$ = 8.0 Hz, $^3J_{H,H}$ = 6.0 Hz, 1H, H-6), 4.51 (dd, $^3J_{H,H}$ = 8.0 Hz, $^3J_{H,H}$ = 3.0 Hz, 1H, H-4), 7.02 (t, $^3J_{H,H}$ = 7.5 Hz, 1H, Ar), 7.16 (d, $^3J_{H,H}$ = 7.5 Hz, 2H, Ar), 7.24 (d, $^3J_{H,H}$ = 7.5 Hz, 2H, Ar), 7.31-7.38 (m, 3H, H-7, Ar), 7.61 (d, $^3J_{H,H}$ = 7.5 Hz, 2H, Ar), 9.75 (s, 1H, H-1). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 20.7 (CH_3), 35.0 (CH_2), 35.4 (CH-6),

51.3 (OCH_3), 54.0 (CH-4), 81.5 (C-3a), 117.2, 122.3, 126.5, 128.5, 128.8 (CH_{Ar}), 136.5, 138.8, 139.8 (C_{Ar}), 157.5 (C=O), 164.2 (C-7a), 173.4 ($\underline{C}O_2CH_3$). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3326 (w), 3026 (w), 2947 (w), 1720 (m), 1667 (w), 1587 (s), 1556 (m), 1495 (m), 1484 (m), 1328 (m), 1273 (m), 1200 (m), 1172 (m), 1092 (m), 820 (m), 752 (s), 694 (m), 655 (m). MS (EI, 70 eV): *m/z* (%) = 364 (21) [M^++1], 363 (100) [M^+], 303 (60), 276 (20), 245 (49), 207 (65), 185 (14), 129 (33), 91 (17), 77 (25), 51 (8). HRMS (ESI): calcd $C_{21}H_{22}N_3O_3$ ([M+1]$^+$) 364.1656, found 364.1651. Anal. Calcd for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56, found: C, 69.036; H, 6.016; N, 11.421.

6-(Naphthalen-2-yl)-2-phenyl-4-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-*b*]pyridin-3(2H)-one (59g)



Starting from 6-(naphthalen-2-yl)-2-phenyl-4-(tri fluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3(2*H*)-one **2aj** (405 mg, 1 mmol), **59g** was isolated as colorless solid (233 mg, 57%); mp 120-122 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.98 (dt, $^3J_{H,H}$ = 13.2 Hz, $^3J_{H,H}$ = 9.6 Hz, 1H, H_a-5), 2.29-2.34 (m, 1H, H_b-5), 3.64-3.82 (m, 1H, H-4), 4.73-4.77 (m, 1H, H-6), 7.06 (t, $^3J_{H,H}$ = 7.4 Hz, 1H, Ar), 7.34-7.39 (m, 2H, Ar), 7.49-7.65 (m, 6H, H-7, Ar), 7.92-7.97 (m, 4H, Ar), 9.94 (s, 1H, H-1). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 31.8 (q, $^3J_{C,F}$ = 5 Hz, CH_2), 35.0 (q, $^2J_{C,F}$ = 29.5 Hz, $\underline{C}CF_3$), 54.0 (C-6), 77.0 (C-3a), 117.7, 122.6, 124.9, 125.2, 126.0, 126.3 (CH_{Ar}), 126.9 (q, $^1J_{C,F}$ = 280.0 Hz, CF_3), 127.6, 127.8, 128.1, 128.5 (CH_{Ar}), 132.6, 132.9, 139.3, 139.6 (C_{Ar}), 159.0 (C=O), 163.6 (C-7a). ^{19}F NMR (282 MHz, DMSO-d_6): δ = -67.09 (s). IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3054 (w), 2929 (w), 1568 (m), 1556 (m), 1496 (m), 1365 (w), 1316 (m), 1260 (m), 1195 (m), 1151 (m), 1115 (s), 1002 (w), 858 (m), 817 (m), 745 (s), 692 (m). MS (EI, 70 eV): *m/z* (%) = 410 (28) [M^++1], 409 (100) [M^+], 235 (33), 174 (23), 154 (19), 77 (36). HRMS (EI): calcd $C_{23}H_{18}F_3N_3O$ ([M]$^+$) 409.13965, found 409.13914. Anal. Calcd for $C_{23}H_{18}F_3N_3O$: C, 67.48; H, 4.43; N, 10.26. Found: C, 67.61; H, 4.39; N, 9,98.

Appendix 2: Crystallographic data

Crystal data and structure refinement for 2g

Identification code	**is_ls164**
Empirical formula	$C_{17}H_{10}F_3N_3OS \cdot C_2H_6OS$
Formula weight	439.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group (H.-M.)	P-1
Space group (Hall)	-P 1
Unit cell dimensions:	a = 10.3182 (4) Å α = 115.6070 (10)°
	b = 10.3297 (2) Å β = 99.4920 (10)°
	c = 10.9223 (2) Å γ = 104.1050 (10)°
Volume	968.33 (5) $Å^3$
Z	2
Calculated density	1.507 mg/m^3
Absorption coefficient	0.32 mm^{-1}
F(000)	452
Crystal size	0.54 x 0.18 x 0.06 mm
Θ range for data collection	2.34° to 30.00°
Index ranges	$-14 \leq h \leq 14$, $-14 \leq k \leq 14$, $-15 \leq l \leq 15$
Reflections collected	20690
Independent reflections	4823 [R(int) = 0.0276]
Absorption correction	Multi-scan
Max. and min. transmission	0.9808 and 0.8443
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5623 / 0 / 268
Goodness-of-fit on F^2	1.035
Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0910
R indices (all data)	R1 = 0.0450, wR2 = 0.0960

Crystal data and structure refinement for 37f

Identification code	**is_ls265**
Empirical formula	$C_{28}H_{24}F_3N_3O_9$
Formula weight	603.50
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorombic
Space group (H.-M.)	$P2_12_12_1$
Space group (Hall)	P2*ac*2*ab*
Unit cell dimensions:	a = 7.0420 (6) Å α = 90°
	b = 11.1180 (11) Å β = 90°
	c = 34.714 (4) Å γ = 90°
Volume	2717.9 (5) $Å^3$
Z	4
Calculated density	1.475 mg/m^3
Absorption coefficient	0.124 mm^{-1}
F(000)	1248
Crystal size	0.35 x 0.09 x 0.06 mm
Θ range for data collection	2.54° to 30.00°
Index ranges	$-9 \leq h \leq 7$, $-15 \leq k \leq 15$, $-48 \leq l \leq 48$
Reflections collected	42455
Independent reflections	5242 [R(int) = 0.0582]
Absorption correction	Multi-scan
Max. and min. transmission	0.9926 and 0.9579
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7921 / 0 / 392
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R1 = 0.0482, wR2 = 0.0796
R indices (all data)	R1 = 0.0946, wR2 = 0.0943

Crystal data and structure refinement for 37g

Identification code	**is_ls054**
Empirical formula	$C_{31}H_{26}F_5N_3O_9$
Formula weight	679.55
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1$
Space group (Hall)	P2*yb*
Unit cell dimensions:	a = 12.3854 (4) Å α = 90°
	b = 8.1987 (3) Å β = 96.4430 (10)°
	c = 14.8841 (5) Å γ = 90°
Volume	1501.85 (9) $Å^3$
Z	2
Calculated density	1.503 mg/m^3
Absorption coefficient	0.131 mm^{-1}
F(000)	700
Crystal size	0.46 x 0.41 x 0.11 mm
Θ range for data collection	2.75° to 31.54°
Index ranges	$-8 \leq h \leq 18$, $-11 \leq k \leq 12$, $-21 \leq l \leq 21$
Reflections collected	19825
Independent reflections	8700 [R(int) = 0.0164]
Absorption correction	Multi-scan
Max. and min. transmission	0.9858 and 0.9423
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9515 / 1 / 436
Goodness-of-fit on F^2	1.018
Final R indices [I>2sigma(I)]	R1 = 0.0355, wR2 = 0.0867
R indices (all data)	R1 = 0.0412, wR2 = 0.0911

Crystal data and structure refinement for 40b

Identification code	**ls079**
Empirical formula	$C_{24}H_{20}F_3N_3O_5 \cdot C_2H_6O$
Formula weight	533.50
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1$
Space group (Hall)	P2*yb*
Unit cell dimensions:	a = 5.9439 (7) Å α = 90°
	b = 20.179 (3) Å β = 101.546 (7)°
	c = 10.5014 (13) Å γ = 90°
Volume	1234.0 (3) $Å^3$
Z	2
Calculated density	1.436 mg/m^3
Absorption coefficient	0.117 mm^{-1}
F(000)	556
Crystal size	0.74 x 0.14 x 0.12 mm
Θ range for data collection	2.83° to 32.50°
Index ranges	$-7 \leq h \leq 8$, $-27 \leq k \leq 30$, $-15 \leq l \leq 15$
Reflections collected	16244
Independent reflections	6406 [R(int) = 0.0234]
Absorption correction	Multi-scan
Max. and min. transmission	0.9861 and 0.9182
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8263 / 1 / 360
Goodness-of-fit on F^2	1.018
Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.0903
R indices (all data)	R1 = 0.0655, wR2 = 0.1023

Crystal data and structure refinement for 40t

Identification code	**is_ls278**
Empirical formula	$C_{25}H_{18}F_3N_3O_7 \cdot H_2O$
Formula weight	547.44
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	$P2_1$
Space group (Hall)	P2*yb*
Unit cell dimensions:	a = 7.8151 (3) Å α = 90°
	b = 11.9529 (4) Å β = 90.141 (2)°
	c = 24.9115 (9) Å γ = 90°
Volume	2327.05 (15) $Å^3$
Z	4
Calculated density	1.563 mg/m^3
Absorption coefficient	0.133 mm^{-1}
F(000)	1128
Crystal size	0.69 x 0.33 x 0.06 mm
Θ range for data collection	0.82° to 32.50°
Index ranges	$-11 \leq h \leq 11$, $-18 \leq k \leq 15$, $-37 \leq l \leq 37$
Reflections collected	42695
Independent reflections	12403 [R(int) = 0.0296]
Absorption correction	Multi-scan
Max. and min. transmission	0.9921 and 0.9139
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	14820 / 7 / 743
Goodness-of-fit on F^2	1.044
Final R indices [I>2sigma(I)]	R1 = 0465, wR2 = 0.0973
R indices (all data)	R1 = 0624, wR2 = 0.1044

Crystal data and structure refinement for 42g

Identification code	**is_ls062**
Empirical formula	$C_{26}H_{22}F_5N_3O_6$
Formula weight	567.47
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorombic
Space group (H.-M.)	$P2_12_12_1$
Space group (Hall)	P2*ac*2*ab*
Unit cell dimensions:	a = 10.0280 (2) Å α = 90°
	b = 11.7016 (3) Å β = 90°
	c = 20.3084 (5) Å γ = 90°
Volume	2383.06 (10) $Å^3$
Z	4
Calculated density	1.582 mg/m^3
Absorption coefficient	0.138 mm^{-1}
F(000)	1168
Crystal size	0.27 x 0.12 x 0.06 mm
Θ range for data collection	2.66° to 30.00°
Index ranges	$-12 \leq h \leq 14$, $-16 \leq k \leq 14$, $-28 \leq l \leq 28$
Reflections collected	28834
Independent reflections	5026 [R(int) = 0.0607]
Absorption correction	Multi-scan
Max. and min. transmission	0.9917 and 0.9636
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6943 / 0 / 374
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0539, wR2 = 0.1104
R indices (all data)	R1 = 0892, wR2 = 0.1280

Crystal data and structure refinement for 51b

Identification code	**ch_ls293**
Empirical formula	$C_{27}H_{20}F_3N_3O$
Formula weight	459.46
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Orthorombic
Space group (H.-M.)	P*bca*
Space group (Hall)	-P2*ac*2*ab*
Unit cell dimensions:	a = 20.2511 (4) Å α = 90°
	b = 10.6301 (4) Å β = 90°
	c = 20.8518 (4) Å γ = 90°
Volume	4488.79 (15) $Å^3$
Z	8
Calculated density	1.360 mg/m^3
Absorption coefficient	0.101 mm^{-1}
F(000)	1904
Crystal size	0.53 x 0.35 x 0.20 mm
Θ range for data collection	2.78° to 30.00°
Index ranges	$-28 \leq h \leq 28$, $-14 \leq k \leq 13$, $-29 \leq l \leq 29$
Reflections collected	61693
Independent reflections	4572 [R(int) = 0.0412]
Absorption correction	Multi-scan
Max. and min. transmission	0.9800 and 0.9482
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6538 / 0 / 307
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0415, wR2 = 0.0951
R indices (all data)	R1 = 0.0707, wR2 = 0.1146

Crystal data and structure refinement for 59a

Identification code	**is_ls0133**
Empirical formula	$C_{14}H_{14}F_3N_3O \cdot CH_4O$
Formula weight	329.32
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group (H.-M.)	P21/*c*
Space group (Hall)	-P2*ybc*
Unit cell dimensions:	a = 5.070 (5) Å α = 90°
	b = 8.125 (8) Å β = 92.82 (3)°
	c = 36.71 (3) Å γ = 90°
Volume	1511 (2) $Å^3$
Z	4
Calculated density	1.448 mg/m^3
Absorption coefficient	0.122 mm^{-1}
F(000)	688
Crystal size	0.74 x 0.15 x 0.14 mm
Θ range for data collection	4.45° to 29.00°
Index ranges	$-6 \leq h \leq 6$, $-11 \leq k \leq 10$, $-50 \leq l \leq 47$
Reflections collected	14346
Independent reflections	3048 [R(int) = 0.0378]
Absorption correction	Multi-scan
Max. and min. transmission	0.9831 and 0.9149
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3960 / 0 / 222
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0577, wR2 = 0.1358
R indices (all data)	R1 = 0.0762, wR2 = 0.1419